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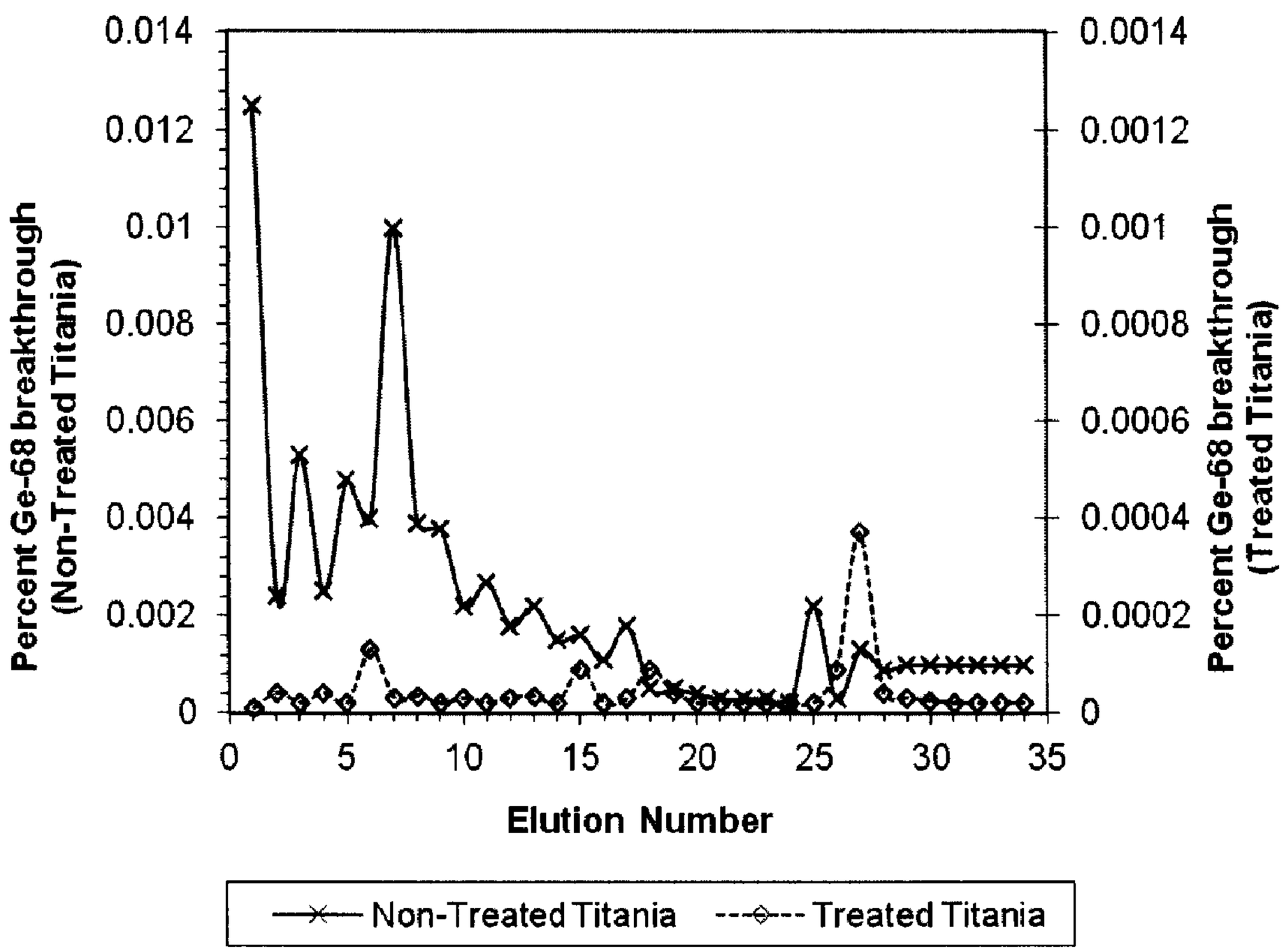
(54) **Titre : PROCEDE DE PRETRAITEMENT D'UN ADSORBANT POUR UNE SEPARATION CHROMATOGRAPHIQUE**
(54) **Title: METHOD OF PRE-TREATING AN ADSORBENT FOR A CHROMATOGRAPHIC SEPARATION**



(57) **Abrégé/Abstract:**
A method of treating an adsorbent for a chromatographic separation. The method involves sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide and washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter to produce a treated adsorbent. The treated adsorbent can be used in a method of isolating a daughter radioisotope from a daughter radioisotope that is produced from the parent radioisotope by radioactive decay.

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(54) **Title**: METHOD OF PRE-TREATING AN ADSORBENT FOR A CHROMATOGRAPHIC SEPARATION

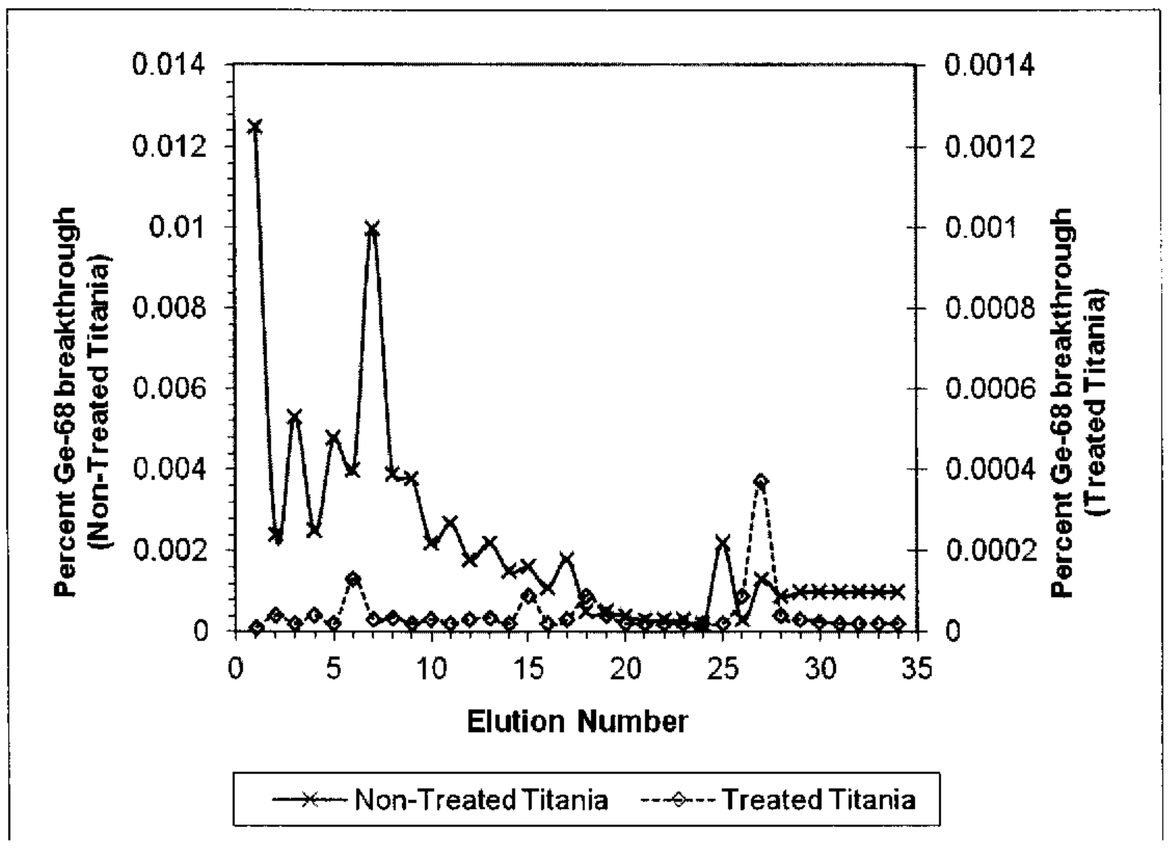

FIG. 5

(57) **Abstract**: A method of treating an adsorbent for a chromatographic separation. The method involves sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide and washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter to produce a treated adsorbent. The treated adsorbent can be used in a method of isolating a daughter radioisotope from a daughter radioisotope that is produced from the parent radioisotope by radioactive decay.

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METHOD OF PRE-TREATING AN ADSORBENT FOR A CHROMATOGRAPHIC SEPARATION

FIELD OF THE INVENTION

[0001] The present invention provides a method of pre-treating an adsorbent for use in a chromatographic separation. In particular, the present invention relates to a method of pre-treating a metal oxide absorbent for use in separating a daughter radioisotope from a parent radioisotope.

BACKGROUND OF THE INVENTION

[0002] Radionuclide generators are commonly used for the isolation of a daughter radioisotope from a parent radioisotope based on differences in the adsorption of the two radionuclides to an adsorbent in the presence of an eluting solvent. A problem associated with the adsorbents used in these generators is that they have fragile edges that tend to flake off as a powder during elution of the desired daughter radionuclide, and clog a filtration membrane located at the distal end of the chromatography column in which the adsorbent is disposed. As a result, the performance of the generator can become significantly impeded. Furthermore, as the parent radionuclide may be adsorbed to the powder that is formed during elution of the daughter radioisotope, the purity of the eluted daughter radionuclide may be significantly compromised.

[0003] There is therefore a need for a method of pre-treating particles of an adsorbent used in radionuclide generators, which removes the fragile edges disposed along the periphery of the particles, to improve the performance of the radionuclide generators and increase the purity of the daughter radionuclide eluted from the generators.

SUMMARY OF THE INVENTION

[0004] The present invention provides a method of pre-treating an adsorbent for use in a chromatographic separation. In particular, the present invention relates to a method of pre-

treating a metal oxide absorbent for use in separating a daughter radioisotope from a parent radioisotope.

[0005] In a first aspect, the present invention provides a method of treating an adsorbent for a chromatographic separation, comprising:

sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide;

washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter, thereby producing a washed, treated adsorbent.

[0006] In a second aspect, the present invention provides a method of isolating a daughter radioisotope from a parent radioisotope, the daughter radioisotope produced from the parent radioisotope by radioactive decay, the method comprising:

adsorbing the parent radioisotope onto particles of an inorganic metal oxide, in particular irregularly-shaped particles of the inorganic metal oxide, having a smoothened surface to produce inorganic metal oxide particles comprising adsorbed parent radioisotope;

allowing a portion of the parent radioisotope to decay to the daughter radioisotope, and

eluting a solution of the daughter radioisotope from the inorganic metal oxide particles comprising adsorbed parent radioisotope, thereby isolating the daughter radioisotope from the parent radioisotope.

[0007] In a third aspect, the present invention provides a method of isolating a daughter radioisotope from a parent radioisotope, the daughter radioisotope produced from the parent radioisotope by radioactive decay, the method comprising:

sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide;

washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter, and

using the washed, smoothened particles of the inorganic metal oxide to isolate the daughter radioisotope from the parent radioisotope.

[0008] In a fourth aspect, the present invention provides a method of isolating a compound of interest from a crude sample, comprising:

sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide;

washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter, and

using the washed, smoothened particles of the inorganic metal oxide to isolate the compound of interest from the crude sample.

[0009] In a fifth aspect, the present invention provides a composition comprising irregularly-shaped particles of an inorganic oxide having a smoothened surface.

[0010] In a sixth aspect, the present invention provides a chromatographic column for isolating a compound of interest, the chromatographic column packed with spherically-shaped or irregularly-shaped particles of an inorganic oxide having a smoothened surface, and comprising an inlet for an eluent and an outlet for an eluate.

[0011] The method of treating an adsorbent of the first aspect of the present invention is generally useful for the preparation of different types of column packings, such as packings for a chromatography column of an HPLC system or a radionuclide generator. This method produces a metal oxide adsorbent having improved mechanical stability, which can form more homogeneous column packings, and require a reduced pressure for eluting compounds during a chromatographic separation. The particles of the metal oxide adsorbent produced by the

methods of the present invention can also result in lower breakthrough of a parent radionuclide during the chromatographic separation of a daughter radionuclide from the parent radionuclide and reduced plugging of the chromatography column used in the chromatographic separation as a result of the reduction in fine particulate matter derived from the particles of the adsorbent.

BRIEF DESCIPTION OF THE DRAWINGS

[0012] These and other features of the invention will become more apparent from the following description in which reference is made to the appended drawings wherein:

[0013] **FIG. 1** illustrates an example of a radioisotope generator that can be used in the method of isolating a daughter radioisotope according to the present invention.

[0014] **FIG. 2A** illustrates an electron micrograph of irregularly-shaped particles of titania having fragile edges, which have been sieved to a particle size of 150 to 250 microns.

[0015] **FIG. 2B** illustrates an electron micrograph of irregularly-shaped particles of titania having smoothened edges produced by treating the particles shown in **FIG. 2A** with the sonication step of the treatment method of the present invention.

[0016] **FIG. 3** illustrates an X-ray diffraction pattern of an anatase standard (top graph) and X-ray diffraction patterns of anatase titania particles produced using examples of the treatment method of the present invention, which include a baking step of 400°C, 500°C or 600°C.

[0017] **FIGS. 4A-B** illustrate a plot of the amount of ^{68}Ge breakthrough as a function of elution number and a plot of the values of percent yield of ^{68}Ga as a function of elution number, respectively, based on eluted samples obtained with a 33 mCi radionuclide generator using irregularly-shaped particles of anatase titania adsorbent, which were pre-treated according to the treatment method of the present invention.

[0018] **FIG. 5** illustrates the amount of ^{68}Ge co-eluted with ^{68}Ga (breakthrough) as a function of elution number based on elutions conducted with a) a 25 mCi radionuclide generator using untreated irregularly-shaped particles of anatase titania as adsorbent ("Non-Treated Titania") and b) a 33 mCi radionuclide generator using irregularly-shaped particles of anatase titania adsorbent

that were pre-treated according to the treatment method of the present invention ("Treated Titania").

DETAILED DESCRIPTION OF THE INVENTION

[0019] The present invention provides a method of pre-treating an adsorbent for use in a chromatographic separation. In particular, the present invention relates to a method of pre-treating a metal oxide absorbent for use in separating a daughter radioisotope from a parent radioisotope.

[0020] The present invention relates to a method of treating an adsorbent for a chromatographic separation, comprising:

sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide, and

washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter, thereby producing a treated adsorbent.

[0021] The present invention also relates to a composition comprising irregularly-shaped particles of an inorganic oxide having a smoothened surface. In one example, the inorganic metal oxide in the composition can have a particle size of from about 10 μm to about 300 μm, or any value or sub-range therebetween. In another example, the particles have been pre-baked at a temperature of from about 400-600°C, or any value or sub-range therebetween, for about 1 to about 2 hours.

[0022] The particles of the inorganic metal oxide prepared according to the treatment method of the present invention can generally be used to isolate a compound of interest from a crude sample, or isolate a daughter radioisotope from a parent radioisotope.

[0023] Accordingly, the present invention provides a method of isolating a compound of interest from a crude sample, or a daughter radioisotope from a parent radioisotope, the method comprising:

I) adsorbing the parent radioisotope onto particles of an inorganic metal oxide, in particular, irregularly-shaped particles of an inorganic metal oxide, having a smoothened surface, to produce inorganic metal oxide particles comprising adsorbed parent radioisotope;

allowing a portion of the parent radionuclide to decay to the daughter radionuclide, and

eluting a solution of the daughter radioisotope from the inorganic metal oxide particles comprising adsorbed parent radioisotope, thereby isolating the daughter radioisotope from the parent radioisotope; or

II) adsorbing the crude sample onto particles of an inorganic metal oxide, in particular, irregularly-shaped particles of an inorganic metal oxide, having a smoothened surface, to produce inorganic metal oxide particles comprising adsorbed crude sample, and

eluting a solution of the compound of interest from the inorganic metal oxide particles comprising adsorbed crude sample, thereby isolating the compound of interest from the crude sample.

[0024] In another aspect, the present invention provides a method of isolating a compound of interest from a crude sample, or a method of isolating a daughter radioisotope from a parent radioisotope, which comprises:

sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide;

washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter, and

using the washed, smoothened particles of the inorganic metal oxide to isolate the compound of interest from the crude sample or the daughter radioisotope from the parent radioisotope.

[0025] In one example, the step of using comprises:

I) adsorbing the parent radioisotope onto the washed, smoothened particles of the inorganic metal oxide to produce inorganic metal oxide particles comprising adsorbed parent radioisotope;

allowing a portion of the parent radionuclide to decay to the daughter radionuclide, and

eluting a solution of the daughter radioisotope from the inorganic metal oxide particles comprising adsorbed parent radioisotope, thereby isolating the daughter radioisotope from the parent radioisotope; or

II) adsorbing the crude sample onto the washed, smoothened particles of the inorganic metal oxide to produce inorganic metal oxide particles comprising adsorbed crude sample, and

eluting a solution of the compound of interest from the inorganic metal oxide particles comprising adsorbed crude sample, thereby isolating the compound of interest from the crude sample.

[0026] In another example, the step of using comprises:

I) adsorbing the parent radioisotope onto a packed layer of the washed, smoothened particles of the inorganic metal oxide to produce a packed layer of inorganic metal oxide particles comprising adsorbed parent radioisotope;

allowing a portion of the parent radionuclide to decay to the daughter radionuclide, and

eluting a solution of the daughter radioisotope from the packed layer of the inorganic metal oxide particles comprising adsorbed parent radioisotope, thereby isolating the daughter radioisotope from the parent radioisotope; or

II) adsorbing the crude sample onto a packed layer of the washed, smoothened particles of the inorganic metal oxide to produce a packed layer of inorganic metal oxide particles comprising adsorbed crude sample, and

eluting a solution of the compound of interest from the packed layer of the inorganic metal oxide particles comprising adsorbed crude sample, thereby isolating the compound of interest from the crude sample.

[0027] The washed, smoothened particles produced according to the treatment method of the present invention can be used to form a packed sorbent layer within a chromatography column that forms part of a generator for eluting a daughter radioisotope from a parent radioisotope. Examples of radioisotope generators that can be used in the methods of the present invention are described in U.S. Patent Nos. 7,700,926 and 7,091,494, the disclosures of which are incorporated by reference herein.

[0028] **FIG. 1** illustrates an example of a radioisotope generator **10** that can be used in the method of isolating a daughter radioisotope of the second and the third aspects of the present invention, which includes a housing having a first end **30**, a second end **40**, and a wall **50** extending between the first end and the second end. The housing has an internal volume **60** and a surface that comprises an entry port **70** and an exit port **80.** A chromatography column **90** is disposed within the internal volume **60** of the housing, which is packed with spherically-shaped or irregularly-shaped particles of inorganic metal oxide particles, which have a smoothened surface prepared according to the treatment method of the present invention and are loaded with the parent radioisotope of the daughter radioisotope. The chromatography column **90** is surrounded by a radiation shield **20** formed of lead, tungsten or depleted uranium.

[0029] The chromatography column **90** includes an inlet **110** for an eluent for eluting the daughter radioisotope from the parent radioisotope and an outlet **120** for an eluate containing the daughter radioisotope.

[0030] The radioisotope generator **10** includes a fluid reservoir **130** having a septum **135** and containing a supply of eluent, which is connected to a first fluid conduit **140** having an inlet **150**

and an outlet **160**. The outlet **160** of the first fluid conduit **140** is connected to and extends from the inlet **110** of the chromatography column **90** to the entry port **70** of the generator **10**. The inlet **150** of the first fluid conduit **140** is attached to a hollow, elongate spike body **145** in fluid communication with the first fluid conduit **140**, which has a pointed end capable of piercing the septum **135** of the fluid reservoir **130**. The outlet of the chromatography column **90** is connected to a second fluid conduit **170** having an inlet **180** and an outlet **190**. The inlet **180** of the second fluid conduit **170** is connected to and extends from the outlet **120** of the chromatography column **90** to the exit port **80** of the generator **10**.

[0031] The radioisotope generator may also include a container **200**, such as an evacuated container, for collecting the eluate from the chromatography column **90**. The outlet **190** of the second fluid conduit **170** may be attached to a needle **220** for piercing the closure **210** of the container **200**. A filter **215** (such as a 0.45 micron filter) may also be connected between the outlet **190** of the second fluid conduit **170** and the needle **220** to remove particulate matter. The container **200** is optionally disposed within a radiation shielding material (not shown).

[0032] The reservoir **130** contains a supply of eluent and includes an outlet **230** for delivery of the eluent to the inlet **150** of the first fluid conduit **140** and optionally an air inlet (not shown) that allows air from the atmosphere to apply pressure to eluent in the reservoir.

[0033] The eluent is forced through the chromatography column using either an evacuated container as the container **200**, or by applying a positive pressure to the supply of the eluent in the reservoir **130**, or both.

[0034] The present invention, therefore provides a chromatographic column for eluting a daughter radioisotope from a parent radioisotope, the chromatographic column packed with spherically-shaped or irregularly-shaped particles of an inorganic oxide having a smoothened surface and comprising an inlet for an eluent for eluting the daughter radioisotope from the parent radioisotope and an outlet for an eluate comprising the daughter radioisotope. The irregularly-shaped particles of an inorganic oxide having a smoothened surface can be loaded with the parent radioisotope.

[0035] More particularly, the present invention provides a generator for eluting a daughter radioisotope from a parent radioisotope and for collecting an eluate comprising the daughter radioisotope in a container, the system comprising:

a housing comprising a radiation shield, the housing having a first end, a second end, and a wall extending between the first end and the second end, and the housing having both an internal volume and a surface that comprises an entry port and an exit port;

a chromatographic column disposed within the internal volume of the housing and enclosed within the radiation shield, the chromatographic column comprising spherically-shaped or irregularly-shaped particles of an inorganic oxide having a smoothened surface, the spherically-shaped or irregularly-shaped particles of the inorganic oxide being loaded with the parent radioisotope, the chromatographic column having an inlet for an eluent for eluting the daughter radioisotope from the parent radioisotope and an outlet for the eluate comprising the daughter radioisotope;

a first fluid conduit having an inlet and an outlet, the outlet of the first fluid conduit connected to and extending from the inlet of the chromatographic column to or through the entry port of the housing;

a second fluid conduit having an inlet and an outlet, the inlet of the second fluid conduit connected to and extending from the outlet of the chromatographic column to or through the exit port of the housing, and

a reservoir for holding a supply of eluent, the reservoir having an outlet in fluid communication with the inlet of the first fluid conduit and optionally an air inlet for admission of air from the atmosphere to apply atmospheric air pressure to eluent in the reservoir.

[0036] The generator may further comprise a container having a pierceable closure, for collecting the eluate from the chromatographic column, and a needle connected to the outlet of the second fluid conduit, wherein the closure of the container is pierced by the needle. The container can be disposed external to the housing or within a radiation shielding material.

[0037] The particles of the inorganic metal oxide can be sonicated in the preparation methods of the present invention for a period of about 1 to about 4 hours or any value or subrange therebetween, or for a period of about 1 to about 2 hours or any value or subrange therebetween.

[0038] The solvent used to contain the particles of the metal oxide in the sonication step of the treatment method of the present invention can be one that is capable of conducting ultrasonic waves and is chemically inert to the particles of the metal oxide. Non-limiting examples of such a solvent include without limitation aqueous solutions, such as neutral aqueous solutions, acidic aqueous solutions or basic aqueous solutions; alcohols, such as methanol, ethanol, propanol or isopropanol; and aqueous alcoholic solutions, such as aqueous ethanol solutions or aqueous propanol solutions. Other examples of suitable solvents can be readily determined by one of skill in the art without the use of undue experimentation.

[0039] The treatment method of the present invention may optionally include a step of washing the particles of the inorganic metal oxide to remove fine particulate matter prior to the step of sonicating the particles of the metal oxide.

[0040] The solvent used for washing the particles of the metal oxide or the smoothened particles of the metal oxide may be the same as the one used to contain the particles of the metal oxide in the sonication step, or another solvent that is chemically inert to the particles of the metal oxide or the smoothened particles of the metal oxide and is easily visually decanted.

[0041] The adsorbent of the present invention can have a particle size of from about 10 μm to about 300 μm or any value or subrange therebetween, from about 30 μm to about 100 μm or any value or subrange therebetween, from about 30 μm to about 60 μm or any value or subrange therebetween, from about 50 μm to about 300 μm or any value or subrange therebetween, or from about 100 μm to about 250 μm or any value or subrange therebetween.

[0042] The methods of preparing the adsorbent according to the present invention can optionally include a step of baking the particles of the inorganic metal oxide having fragile edges or the washed, smoothened particles of the inorganic metal oxide at a temperature of from about 400 to about 600°C or any value or subrange therebetween, such as 400°C, 500°C or 600°C for about 1 to about 2 hours or any value or subrange therebetween. The baking step ensures that the

inorganic metal is present predominantly in one form of crystal type. For example, baking particles of titania at a temperature of from about 400 to about 600°C will produce particles of titania in predominantly the anatase form (see **FIG. 3**).

[0043] The particles of the inorganic metal oxide used in the methods of the present invention can be spherically-shaped or irregularly-shaped.

[0044] Examples of the inorganic metal oxide that can be used in the methods of the present invention include, without limitation, titanium oxide (titania), in particular brookite titania, anatase titania, or rutile titania; aluminum oxide; tin oxide; zirconium oxide or silicon dioxide.

[0045] In examples of the method of isolating a daughter radioisotope of the second aspect and the third aspect of the present invention, the parent radioisotope/daughter radioisotope pair are $^{68}Ge/^{68}Ga$, $^{82}Sr/^{82}Rb$, $^{99}Mo/^{99m}Tc$, $^{188}W/^{188}Re$, $^{62}Zn/^{62}Cu$, $^{113}Sn/^{113m}In$, $^{228}Th/^{212}Bi$, or $^{225}Ac/^{221}Fr$. Other examples of radionuclides that can be isolated using the adsorbent of the present invention are described in Lambrecht, R. M. *Radiochimica Acta* 34, 9-24 (1983).

[0046] The particles of the metal oxide can be sonicated by either immersing a reaction vessel containing the particles into the liquid of a common laboratory ultrasonic cleaning bath or by introduction of an ultrasonic generating probe directly into the reaction medium. The ultrasonic frequency used in the step of sonication can be from 20 kHz to 10 MHz or any value or subrange therebetween, or from 20 kHz to 60 kHz or any value or subrange therebetween. In another example, the ultrasonic frequency used in the step of sonication is 40 kHz.

[0047] The particular solvent system used to elute a compound of interest, such as a daughter radionuclide, can be readily determined by one of skill in the art. Examples of specific solvent systems that can be used to elute typical daughter radionuclides are described in Saha, G.B., 1998 "Radionuclide Generators" in *Fundamentals of Nuclear Pharmacy*, 4th Edition, Springer, pp. 65-79.

Examples

[0048] The following example is of a method used to prepare irregularly-shaped anatase crystals of titania for use in isolating a daughter radioisotope from a parent radioisotope.

Crystallization Process

[0049] Into a 1000 mL clean Teflon bottle containing 11.7 g conc HCl was pipetted 10 x 1 mL aliquots of $TiCl_4$ (Alpha Aesar A470-500). The sides of the Teflon bottle were washed with 20 mL of water and the contents of the bottle were swirled to ensure there was no material remaining on the sides of the bottle. The lid of the bottle was tightened and the contents of the bottle were swirled with the bottle being upside down. The bottle was then immediately turned upright and the lid of the bottle was loosened to release any built up pressure. The resulting solution was clear and colourless.

[0050] The Teflon bottle containing the solution of $TiCl_4$ was placed on an orbital shaker and secured. A solution of NH_4OH (54 g NH_4OH/ 200 mL water) was pumped through pre-rinsed Tefzel tubing at a rate of one drop every five seconds into the Teflon bottle containing the $TiCl_4$ solution over a period of 4 - 6 hours with the orbital shaker set at 150 rpm.

Drying & Filtration Process

[0051] A borosilicate sintered filter (medium porosity) was prepared by soaking it in 1N HCl overnight, rinsing it with distilled water and allowing it to dry.

[0052] The titania reaction mixture was filtered through the sintered filter by vacuum without allowing the white cake of titania that was formed to dry out or crack. The filter cake was then washed ten times with 20 mL water just until the water disappeared from the cake, and any remaining water in the cake was drawn out by vacuum. The filter cake was then placed into a furnace to dry overnight at 150°C, and was then baked at 400°C for 2 hours. The resulting filter cake was yellow in colour.

Sieving Process

[0053] The filter containing the dried titania was removed from the furnace and allowed to cool to room temperature. The dried titania was then ground and sieved to a particle size range of from 38 to 53 microns.

Removing Particulate Material

[0054] In order to remove fine particulate material, a solution of 0.1 N HCl was added to the ground titania and the supernatant decanted. This procedure was repeated several times until no further particulate material could be detected.

Sonication

[0055] The washed titania material was then sonicated for 2 hours in 10 to 15 mL of 0.1 N HCl. Fine particulate material was then removed using the procedure detailed above.

Drying Process

[0056] The sonicated material was then dried in an open Teflon bottle in a beaker covered with a watch glass in a furnace at approximately 150°C. The dried material was then transferred into a quartz dish, covered and baked at 500°C for 60 minutes to produce anatase titania as a material having a beige colour. The baked material was then sieved using a 38 μ sieve for one minute.

[0057] The above procedure produced about 3 g of anatase titania.

[0058] **FIG. 2A** illustrates an electron micrograph of irregularly-shaped particles having fragile edges, which can be used as a substrate for the treatment method of the present invention. After being treated according to the treatment method of the present invention, the fragile edges of the irregularly-shaped particles have been removed to leave behind smoothened edges (see **FIG. 2B**).

[0059] **FIG. 3** shows the X-ray diffraction patterns of anatase titania produced by treating irregularly-shaped particles of titania using an example of the treatment method of the present invention, which includes a step of baking the titania particles at a temperature of 400°C, 500°C or 600°C. The X-ray diffraction patterns suggest that larger crystals of anatase titania are formed within the particles of titania as the temperature of baking is increased from 400°C to 600°C.

[0060] **FIG. 4A** illustrates the values of breakthrough of ^{68}Ge measured in samples obtained by eluting a 33 mCi $^{68}Ge/^{68}Ga$ generator according to the present invention with 0.1N HCl. The generator comprised irregularly-shaped particles of anatase titania adsorbent, which were pre-

treated according to the example of the treatment method of the present invention described above. The spikes in values of breakthrough of ^{68}Ge in the plot appear at times that immediately follow periods of days or weeks during which the generator was not in use. In a clinical setting, these particular eluted samples would be discarded. The appearance of these spikes in values of breakthrough of ^{68}Ge is a common phenomenon with radioisotope generators involving long lived radionuclides, and may be caused by radiolysis of the particles of the adsorbent.

[0061] **FIG. 4B** illustrates the values of percent yield of ^{68}Ga as a function of elution number in the same 33 mCi ^{68}Ge/^{68}Ga generator. The value of percent yield for each eluted fraction was determined by dividing the actual amount of Ga-68 eluted from the generator, as measured using a dose calibrator, by the theoretical yield of Ga-68 for each fraction. The theoretical yield of Ga-68 for each fraction was calculated based on Ge-68 activity decay calculations and the time between elutions from the generator. The average value of percent yield of ^{68}Ga for the eluted samples was 72%. The yield may be increased slightly to 75-80% by increasing the volume of eluent used to elute each sample from 5 mL to 10 mL, but will necessitate the use of a larger amount of base to neutralize each collected sample so that the isolated Ga-68 can be used for direct labelling.

[0062] **FIG. 5** illustrates a comparative plot of the first 34 values of breakthrough of ^{68}Ge shown **in FIG. 4A** ("Treated Titania") and the values of breakthrough measured using a similar 25 mCi ^{68}Ge/^{68}Ga generator that includes untreated irregularly-shaped particles of anatase titania as adsorbent ("Non-Treated Titania"). The average value of breakthrough observed using the generator having the treated titania was about 20 fold less than the average value of breakthrough observed using the same generator that included the untreated titania.

[0063] Without wishing to be limited by theory, it is believed that the reduced breakthrough observed with the use of the treated adsorbent of the present invention is at least in part a result of the reduction in the amount of fine particulate matter derived from use of the treated particles of the adsorbent containing adsorbed parent radionuclide, thereby reducing contamination of the eluted ^{68}Ga with the parent radionuclide. The baking step included in the above example of the treatment method used to prepare the adsorbent for the radionuclide generator may also

contribute to the observed reduced breakthrough by ensuring that the titania is predominately in the anatase crystal form.

[0064] One or more currently preferred embodiments have been described by way of example. It will be apparent to persons skilled in the art that a number of variations and modifications can be made without departing from the scope of the invention as defined in the claims.

WHAT IS CLAIMED IS:

1. A method of treating an adsorbent for a chromatographic separation, comprising:

sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide, and

washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter, thereby producing a washed, treated adsorbent.

2. The method according to claim 1, wherein the particles of the inorganic metal oxide are sonicated for a period of about 1 to about 4 hours.

3. The method according to claim 1, wherein the particles of the inorganic metal oxide are sonicated for a period of about 1 to about 2 hours.

4. The method according to any one of claims 1-3, wherein the inorganic metal oxide has a particle size of from about 10 μm to about 300 μm.

5. The method according to any one of claims 1-4, wherein the particles of the inorganic metal oxide are irregularly-shaped.

6. The method according to any one of claims 1-5, further comprising a step of baking the particles of the inorganic metal oxide having fragile edges or the washed, smoothened particles of the inorganic metal oxide at a temperature of from about 400 to about 600°C for about 1 to about 2 hours.

7. The method according to any one of claims 1-6, wherein the inorganic metal oxide is titanium oxide, aluminum oxide, tin oxide, zirconium oxide or silicon dioxide.

8. The method according to claim 7, wherein the inorganic metal oxide is titanium oxide.

9. The method according to any one of claims 1-5, wherein the inorganic metal oxide is titania, and wherein the method further comprises a step of baking the particles of the

inorganic metal oxide having fragile edges or the washed, smoothened particles of the inorganic metal oxide at a temperature of from about 500 to about 600°C for about 1 to about 2 hours to produce particles of anatase titania having fragile edges or washed, smoothened particles of anatase titania.

10. A method of isolating a daughter radioisotope from a parent radioisotope, the daughter radioisotope produced from the parent radioisotope by radioactive decay, the method comprising:

adsorbing the parent radioisotope onto particles of an inorganic metal oxide having a smoothened surface prepared by the method of claim 1, to produce inorganic metal oxide particles comprising adsorbed parent radioisotope;

allowing a portion of the parent radioisotope to decay to the daughter radioisotope; and

eluting a solution of the daughter radioisotope from the inorganic metal oxide particles comprising adsorbed parent radioisotope, thereby isolating the daughter radioisotope from the parent radioisotope.

11. The method according to claim 10, wherein the particles of the inorganic metal oxide have a particle size of about 10 μm to about 300 μm.

12. The method according to claim 10 or 11, wherein the particles of the inorganic metal oxide are sonicated for a period of about 1 to about 4 hours.

13. The method according to claim 10 or 11, wherein the particles of the inorganic metal oxide are sonicated for a period of about 1 to about 2 hours.

14. The method according to any one of claims 10-13, wherein the particles of the inorganic metal oxide are irregularly-shaped.

15. The method according to any one of claims 10-14, further comprising a step of baking the particles of the inorganic metal oxide having fragile edges or the particles of the

inorganic metal oxide having a smoothened surface at a temperature of from about 400°C to about 600°C for about 1 to about 2 hours.

16. The method according to any one of claims 10-15, wherein the inorganic metal oxide is titanium oxide, aluminum oxide, tin oxide, zirconium oxide or silicon dioxide.

17. The method according to claim 16, wherein the inorganic metal oxide is titanium oxide.

18. The method according to any one of claims 10-14, wherein the inorganic metal oxide is titania, and wherein the method further comprises a step of baking the particles of the inorganic metal oxide having fragile edges or the particles of the inorganic metal oxide having a smoothened surface at a temperature of from about 500 °C to about 600°C for about 1 to about 2 hours to produce particles of anatase titania having fragile edges or washed, smoothened particles of anatase titania.

19. The method according to any one of claims 10-18, wherein the parent radioisotope is ^{68}Ge, and the daughter radioisotope is ^{68}Ga.

20. The method according to any one of claims 10-18, wherein the parent radioisotope is ^{82}Sr, and the daughter radioisotope is ^{82}Rb.

21. The method according to any one of claims 10-18, wherein the parent radioisotope is ^{99}Mo, and the daughter radioisotope is ^{99m}Tc.

22. The method according to any one of claims 10-18, wherein the parent radioisotope is ^{188}W, and the daughter radioisotope is ^{188}Re.

23. The method according to claim any one of claims 10-18, wherein the parent radioisotope is ^{62}Zn, and the daughter radioisotope is ^{62}Cu.

24. The method according to claim any one of claims 10-18, wherein the parent radioisotope is ^{113}Sn, and the daughter radioisotope is ^{113m}In.

25. The method according to claim any one of claims 10-18, wherein the parent radioisotope

is ^{228}Th, and the daughter radioisotope is ^{212}Bi.

26. The method according to claim any one of claims 10-18, wherein the parent radioisotope is ^{225}Ac, and the daughter radioisotope is ^{221}Fr.

27. A method of isolating a daughter radioisotope from a parent radioisotope, the daughter radioisotope produced from the parent radioisotope by radioactive decay, the method comprising:

sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide;

washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter, and

using the washed, smoothened particles of the inorganic metal oxide to isolate the daughter radioisotope from the parent radioisotope.

28. The method according to claim 27, wherein the step of using comprises:

adsorbing the parent radioisotope onto the washed, smoothened particles of the inorganic metal oxide to produce inorganic metal oxide particles comprising adsorbed parent radioisotope;

allowing a portion of the parent radioisotope to decay to the daughter radioisotope; and

eluting a solution of the daughter radioisotope from the inorganic metal oxide particles comprising adsorbed parent radioisotope, thereby isolating the daughter radioisotope from the parent radioisotope.

29. The method according to claim 27, wherein the step of using comprises:

adsorbing the parent radioisotope onto a packed layer of the washed, smoothened

particles of the inorganic metal oxide to produce a packed layer of inorganic metal oxide particles comprising adsorbed parent radioisotope;

allowing a portion of the parent radioisotope to decay to the daughter radioisotope; and

eluting a solution of the daughter radioisotope from the packed layer of the inorganic metal oxide particles comprising adsorbed parent radioisotope, thereby isolating the daughter radioisotope from the parent radioisotope.

30. The method according to any one of claims 27-29, wherein the parent radioisotope is ^{68}Ge, and the daughter radioisotope is ^{68}Ga.

31. The method according to any one of claims 27-29, wherein the parent radioisotope is ^{82}Sr, and the daughter radioisotope is ^{82}Rb.

32. The method according to any one of claims 27-29, wherein the parent radioisotope is ^{99}Mo, and the daughter radioisotope is ^{99m}Tc.

33. The method according to any one of claims 27-29, wherein the parent radioisotope is ^{188}W, and the daughter radioisotope is ^{188}Re.

34. The method according to any one of claims 27-29, wherein the parent radioisotope is ^{62}Zn, and the daughter radioisotope is ^{62}Cu.

35. The method according to any one of claims 27-29, wherein the parent radioisotope is ^{113}Sn, and the daughter radioisotope is ^{113m}In.

36. The method according to any one of claims 27-29, wherein the parent radioisotope is ^{228}Th, and the daughter radioisotope is ^{212}Bi.

37. The method according to any one of claims 27-29, wherein the parent radioisotope is ^{225}Ac, and the daughter radioisotope is ^{221}Fr.

38. The method according to any one of claims 27-37, further comprising a step of baking the

particles of the inorganic metal oxide having fragile edges or the washed, smoothened particles of the inorganic metal oxide at a temperature of from about 400 to about 600°C for a period of about 1 to about 2 hours.

39. The method according to any one of claims 27-38, wherein the inorganic metal oxide is titanium oxide, aluminum oxide, tin oxide, zirconium oxide or silicon dioxide.

40. The method according to claim 39, wherein the inorganic metal oxide is titanium oxide.

41. The method according to any one of claims 27-37, wherein the inorganic metal oxide is titania, and wherein the method further comprises a step of baking the particles of the inorganic metal oxide having fragile edges or the washed, smoothened particles of the inorganic metal oxide at a temperature of from about 500 to about 600°C for about 1 to about 2 hours to produce particles of anatase titania having fragile edges or washed, smoothened particles of anatase titania.

42. The method according to any one of claims 27-41, wherein the particles of the inorganic metal oxide are sonicated for a period of about 1 to about 4 hours.

43. The method according to any one of claims 27-42, wherein the particles of the inorganic metal oxide are sonicated for a period of about 1 to about 2 hours.

44. The method according to any one of claims 27-43, further comprising a step of grinding and sieving the inorganic metal oxide to a particle size of from about 10 μm to about 300 μm.

45. A method of isolating a compound of interest from a crude sample, comprising:

sonicating particles of an inorganic metal oxide having fragile edges in the absence of any alkylating or acylating agent to form smoothened particles of the inorganic metal oxide;

washing the smoothened particles of the inorganic metal oxide to remove fine particulate matter, and

using the washed, smoothened particles of the inorganic metal oxide to isolate the compound of interest.

46. The method according to claim 45, wherein the step of using comprises:

adsorbing the crude sample onto the washed, smoothened particles of the inorganic metal oxide to produce inorganic metal oxide particles comprising adsorbed crude sample, and

eluting a solution of the compound of interest from the inorganic metal oxide particles comprising adsorbed crude sample, thereby isolating the compound of interest from the crude sample.

47. The method according to claim 45, wherein the step of using comprises:

adsorbing the crude sample onto a packed layer of the washed, smoothened particles of the inorganic metal oxide to produce a packed layer of inorganic metal oxide particles comprising adsorbed crude sample, and

eluting a solution of the compound of interest from the packed layer of the inorganic metal oxide particles comprising adsorbed crude sample, thereby isolating the compound of interest from the crude sample.

48. The method according to any one of claims 45-47, further comprising a step of baking the particles of the inorganic metal oxide having fragile edges or the washed, smoothened particles of the inorganic metal oxide at a temperature of from about 400 to about 600°C for a period of about 1 to about 2 hours.

49. The method according to any one of claims 45-48, wherein the inorganic metal oxide is titanium oxide, aluminum oxide, tin oxide, zirconium oxide or silicon dioxide.

50. The method according to claim 49, wherein the inorganic metal oxide is titanium oxide.

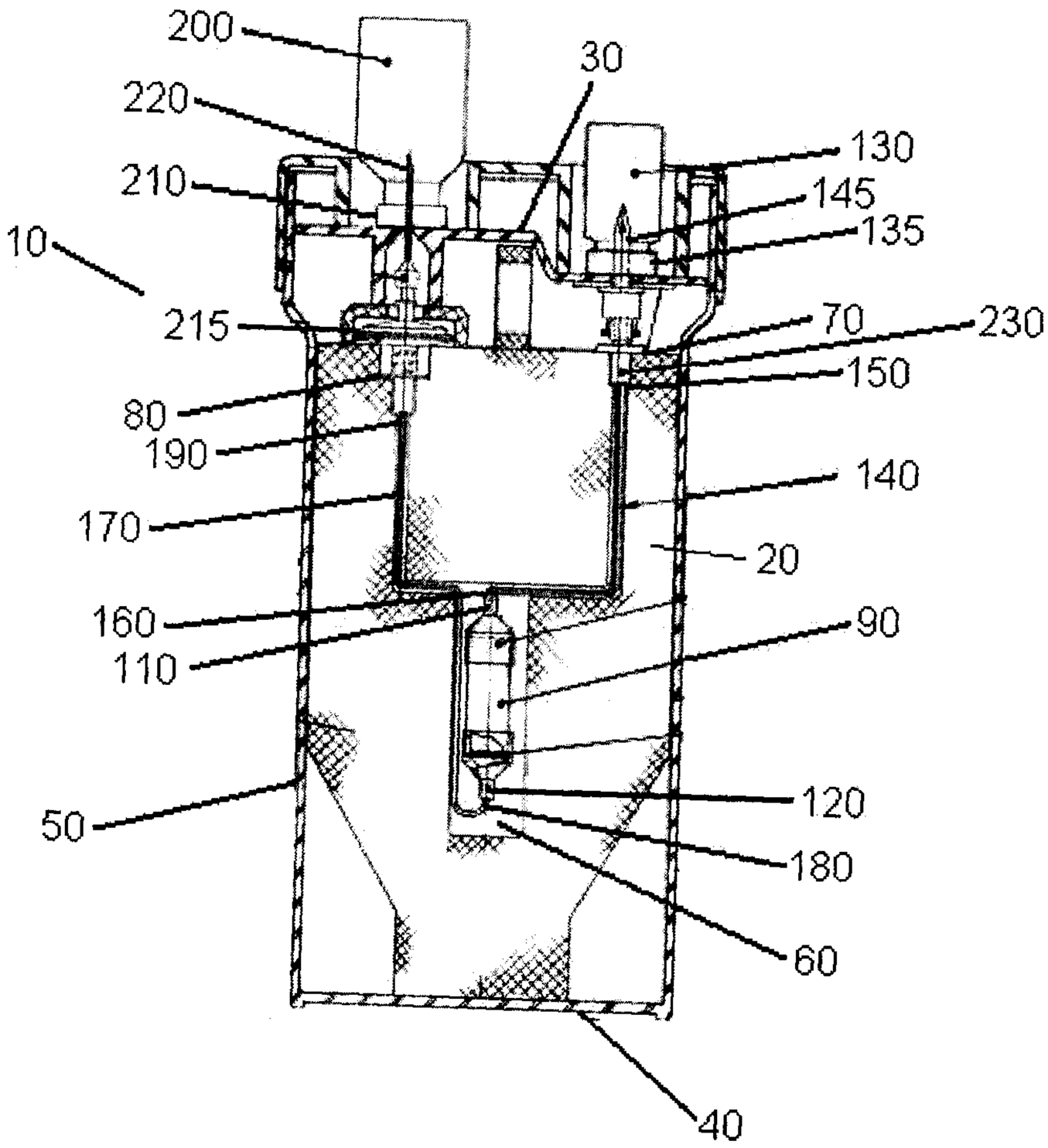
51. The method according to any one of claims 45-47, wherein the inorganic metal oxide is

titania, and wherein the method further comprises a step of baking the particles of the inorganic metal oxide having fragile edges or the washed, smoothened particles of the inorganic metal oxide at a temperature of from about 500 to about 600°C for about 1 to about 2 hours to produce particles of anatase titania having fragile edges or washed, smoothened particles of anatase titania.

52. The method according to any one of claims 45-51, wherein the particles of the inorganic metal oxide are sonicated for a period of about 1 to about 4 hours.

53. The method according to any one of claims 45-51, wherein the particles of the inorganic metal oxide are sonicated for a period of about 1 to about 2 hours.

54. The method according to any one of claims 45-53, further comprising a step of grinding and sieving the inorganic metal oxide to a particle size of from about 10 μm to about 300 μm.


200
30
220
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210
145
135
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150
80
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140
170
20
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90
110
120
50
180
60
40

FIG. 1

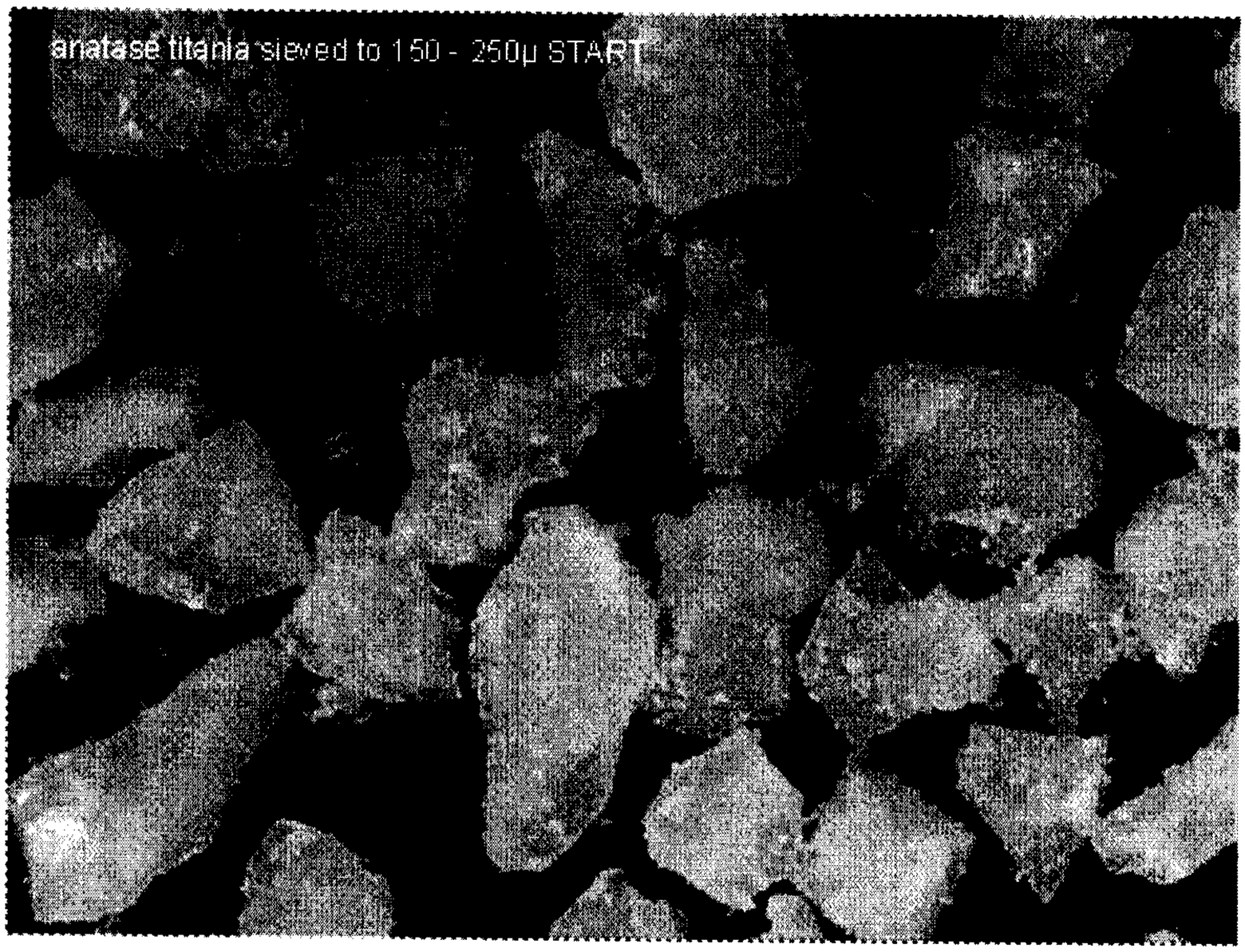
anatase titania sieved to 150 - 250µ START

FIG. 2A

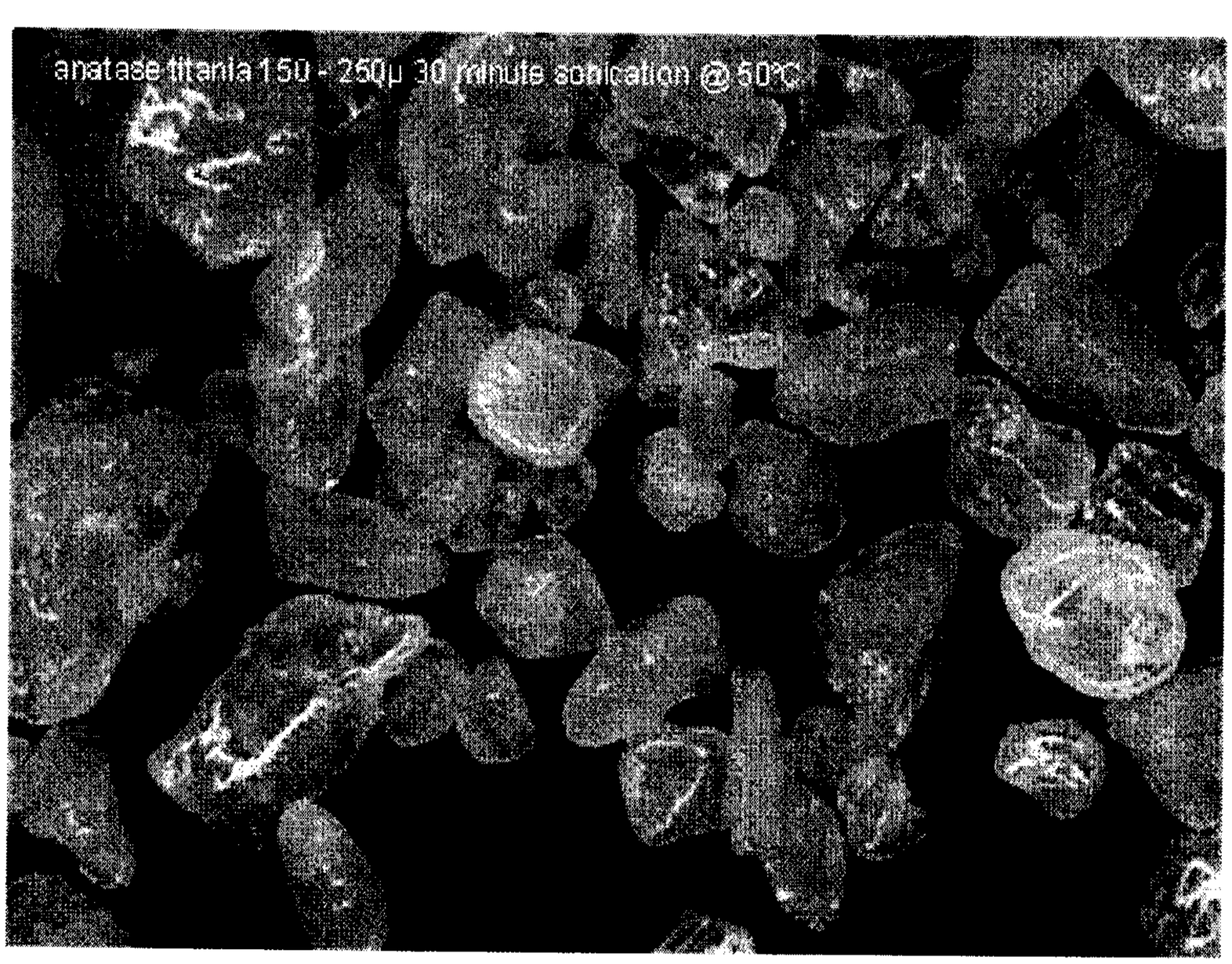
anatase titania 150 - 250µ 30 minute sonication @ 50°C

FIG. 2B

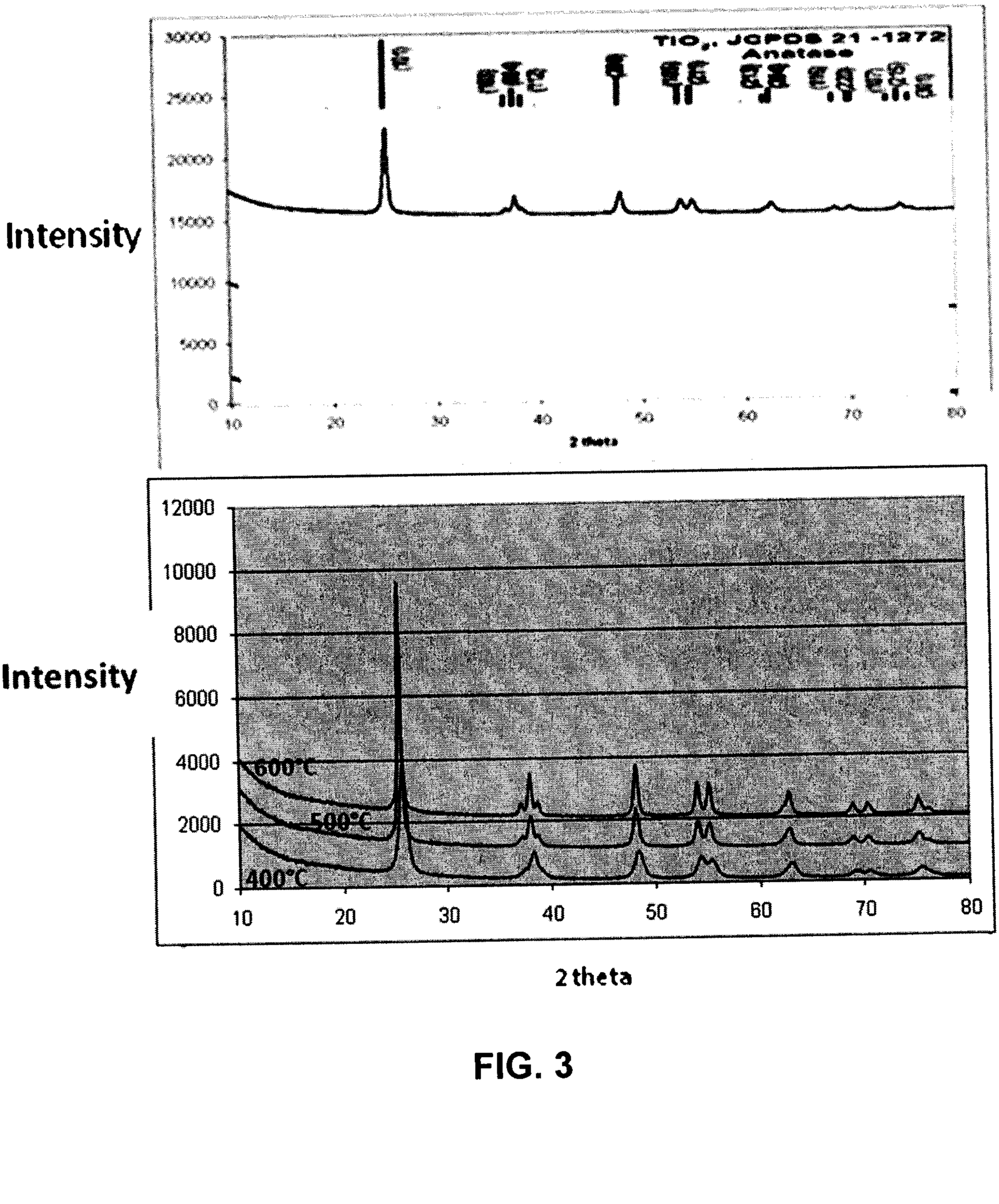
Intensity
TiO2, JCPDS 21-1272
Anatase
30000
25000
20000
15000
10000
5000
0
10
20
30
40
50
60
70
80
2 theta
Intensity
12000
10000
8000
6000
4000
2000
0
600°C
500°C
400°C
10
20
30
40
50
60
70
80
2 theta

FIG. 3

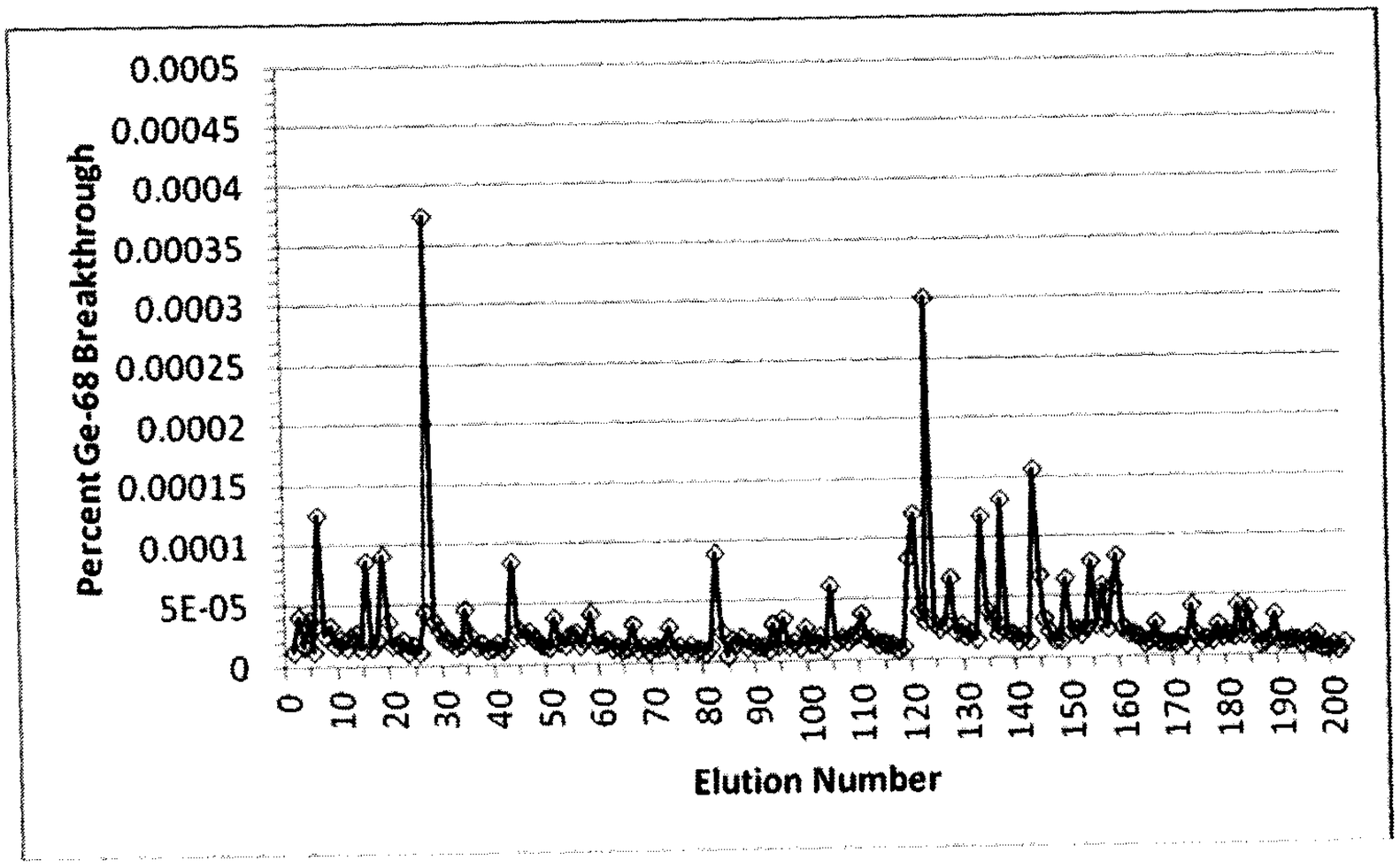
Percent Ge-68 Breakthrough
0.0005
0.00045
0.0004
0.00035
0.0003
0.00025
0.0002
0.00015
0.0001
5E-05
0
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200
Elution Number

FIG. 4A

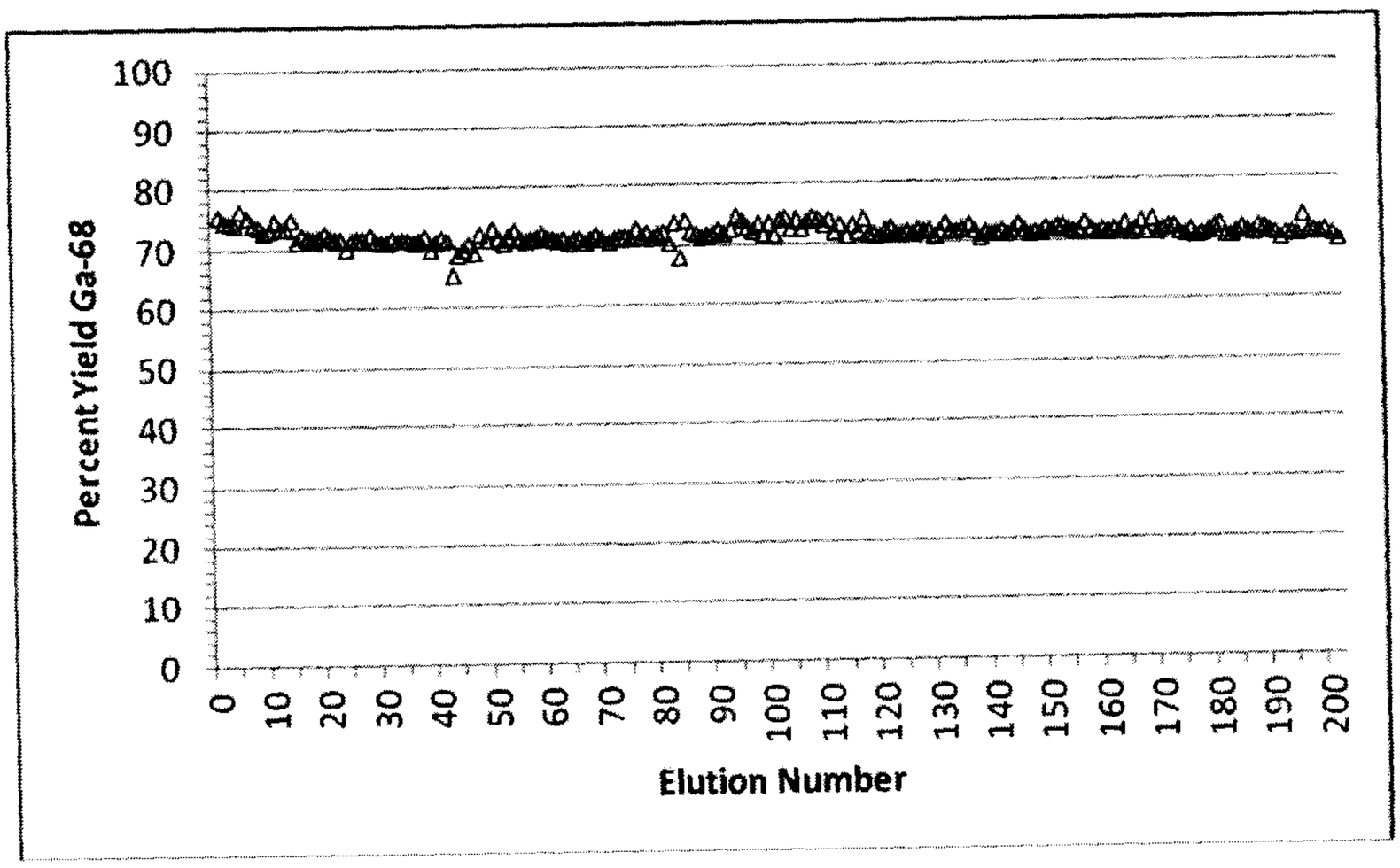
Percent Yield Ga-68
100
90
80
70
60
50
40
30
20
10
0
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200
Elution Number

FIG. 4B

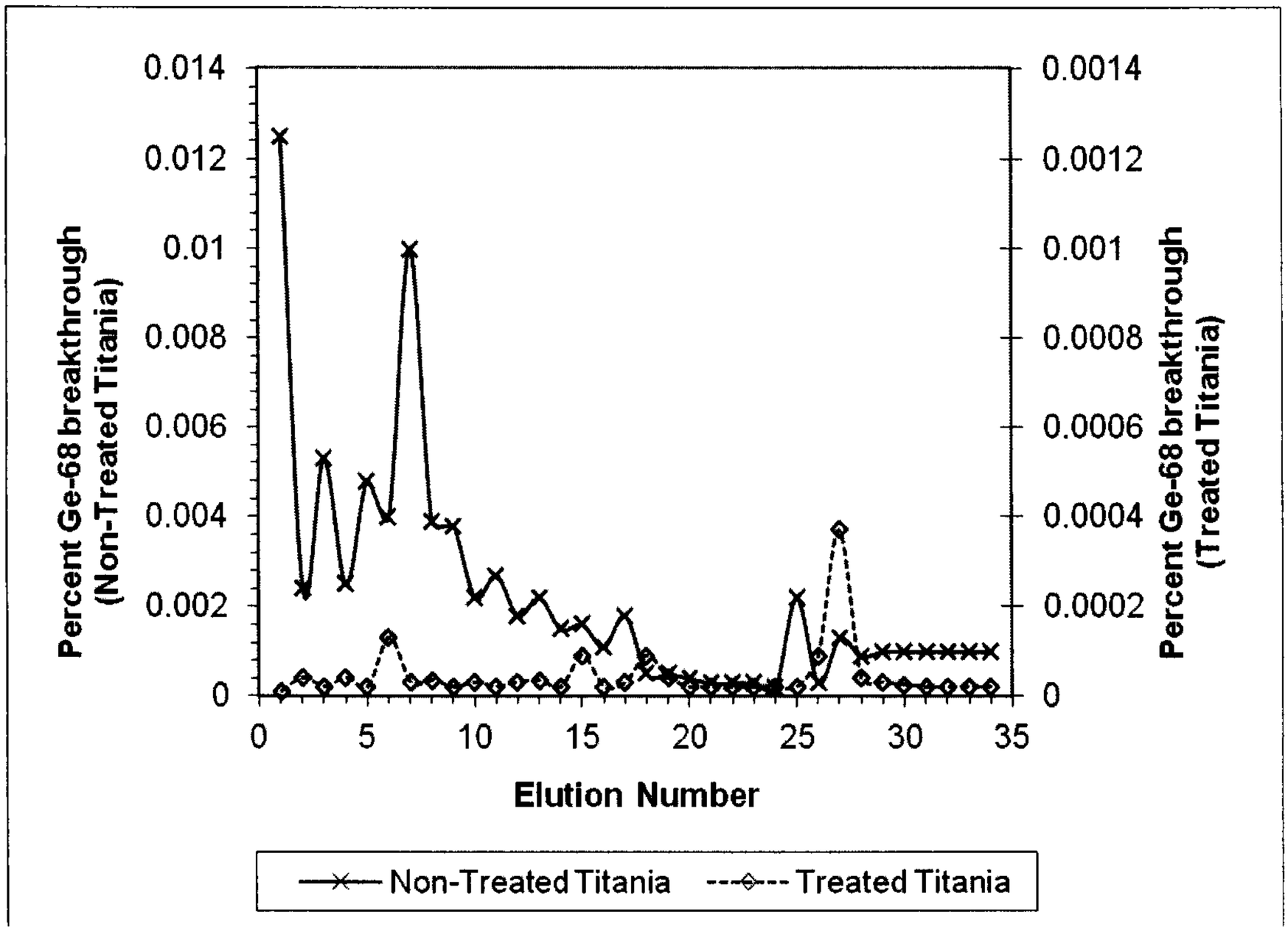
0.014
0.012
0.01
0.008
0.006
0.004
0.002
0
0.0014
0.0012
0.001
0.0008
0.0006
0.0004
0.0002
0
0
5
10
15
20
25
30
35
Percent Ge-68 breakthrough (Non-Treated Titania)
Percent Ge-68 breakthrough (Treated Titania)
Elution Number
Non-Treated Titania
Treated Titania

FIG. 5

0.014
0.012
0.01
0.008
0.006
0.004
0.002
0
0.0014
0.0012
0.001
0.0008
0.0006
0.0004
0.0002
0
0
5
10
15
20
25
30
35
Percent Ge-68 breakthrough (Non-Treated Titania)
Percent Ge-68 breakthrough (Treated Titania)
Elution Number
Non-Treated Titania
Treated Titania