Title: LIQUIDS RICH IN NOBLE GAS AND METHODS OF THEIR PREPARATION AND USE

Abstract: Provided herein is a novel composition for oral administration and delivery of Noble gas, such as xenon or argon. Methods of treating and preventing neuronal or cardiovascular damage with such compositions are also provided. The present invention relates generally to the fields of molecular biology, medicine and nutraceuticals. More particularly, it concerns methods for oral delivery of inert gas compositions, such as Xenon or Argon, for the treatment and prevention of disease.

FIG. 1

[intraventricular Septum; diastole (mm)]

[intraventricular Septum; diastole (mm)]

[LV Posterior wall; diastole (mm)]

[LV Volume; diastole (μl)]

[WT, KO, KO6, KO16, KO16, KO16: control vehicle, Xenon]
TN, TR, TT, TZ, UA, UK, US, UZ, VC, VN, ZA, ZM.

(84) Designated States (unless otherwise indicated, for every
Mnd of regional protection available):


Eurasian (AM, AZ, BY, KG, KZ, RU, TJ),

European (AL, AT, BG, ES, FR, CY, CZ, DE, DK, EE, EL, FI, FR, GR, HR, HU, IE, IS, IT, LT, LU, LV, MT, NL, NO, PL, PT, RO, RS, SK, SI, SL, SK),

OAPI (BF, BJ, CF, CG, CI, CM, GN, GW, KAM, MR, NE, SN, TD, TG),

Published:
— with international search report (Art. 21(3))
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

December 2014
# INTERNATIONAL SEARCH REPORT

**International application No.**

PCT/US2014/030210

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## A. CLASSIFICATION OF SUBJECT MATTER

**IPC(8) - A61K 9/00 (2014.01)**

**USPC - A61K 9/00 (2014.09)**

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

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## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

**IPC(8) - A61K 9/00, 9/10, 9/107, 9/127, 9/48, 9/50, 9/72, 33/00, 47/48 (2014.01)**

**USPC - 423/262; 424/400, 450, 451, 455, 600; 514/937**

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


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

**Orbit, Google Patents, Google Scholar**

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## C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>US 5,496,421 A (GRINSTAFF et al) 12 March 1996 (12.03.1996) entire document</td>
<td>1-8, 10, 12, 13, 15, 19, 20, 30, 44-46</td>
</tr>
<tr>
<td></td>
<td></td>
<td>31-37, 48-57, 59, 63, 65-72, 74, 76, 77, 79, 83, 84</td>
</tr>
</tbody>
</table>

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Further documents are listed in the continuation of Box C.

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* Special categories of cited documents:
  - "A" document defining the general state of the art which is not considered to be of particular relevance
  - "E" earlier application or patent but published on or after the international filing date
  - "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  - "O" document referring to an oral disclosure, use, exhibition or other means
  - "P" document published prior to the international filing date but later than the priority date claimed

"I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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**Date of the actual completion of the international search**

22 September 2014

**Date of mailing of the international search report**

17 OCT 2014

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**Name and mailing address of the ISA/US**

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

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**Authorized officer:**

Blaine R. Copenhaver

PCT Helpdesk: 571-272-4300
PCT DSP: 571-272-7774

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Form PCT/ISA/210 (second sheet) (July 2009)
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. □ Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. □ Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. □ Claims Nos.: 47 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

This International Searching Authority found multiple inventions in this international application, as follows:

See Extra Sheet

1. □ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. □ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. □ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

   1-46, 48-92

4. □ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
<Continued from Box III: Observations where unity of invention is lacking>

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I: Claims 1-43 are drawn to a nutraceutical composition

Group II: Claims 44-46 and 48-92 are drawn to a method of treating a subject

Group III: Claims 93-117 are drawn to a method of making a composition

The inventions listed in Groups I through III do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The special technical features of Group I, a nutraceutical composition, are not present in Groups II and III; the special technical features of Group II, a method of treating a subject, are not present in Groups I and III; and the special technical features of Group III, a method of making a composition, are not present in Groups I and II.

Groups I through III share the technical features of an aqueous composition for oral administration comprising a substantially aqueous component comprising a dissolved Noble gas, a portion of the Noble gas being encapsulated with a water-soluble polymer; and dissolving a Noble gas in an edible oil to produce an edible oil comprising dissolved Noble gas. However, these features do not represent a contribution over the prior art.

Specifically, US 5,498,421 A to Grinstaff et al. teach a composition for oral administration (Col. 1, Lines 14-22; Col. 8, Lines 18-22) comprising a substantially aqueous component comprising a dissolved Noble gas (Col. 7, Line 62-Col. 8, Line 17; Col. 9, Lines 25-32; Col. 14, Lines 19-23), a portion of the Noble gas being encapsulated with a water-soluble polymer (Col. 7, Line 62-Col. 8, Line 17; Col. 9, Lines 25-32; Col. 14, Lines 19-23; Col. 8, Lines 36-55); and dissolving a Noble gas in an edible oil to produce an edible oil comprising dissolved Noble gas (Col. 7, Line 62-Col. 8, Line 17; Col. 9, Lines 25-32).

The inventions listed in Groups I through III therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.

<End Box III: Observations where unity of invention is lacking>