(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 November 2004 (18.11.2004)

(10) International Publication Number
WO 2004/098619 A3

(51) International Patent Classification: A61K 33/24,
A61P 19/08

(21) International Application Number:
PCT/DK2004/000328

(22) International Filing Date: 6 May 2004 (06.05.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PA 2003 00691 7 May 2003 (07.05.2003) DK
PA 2003 00932 20 June 2003 (20.06.2003) DK
60/528,442 9 December 2003 (09.12.2003) US


(72) Inventors: and


(74) Agent: ALBIHNS A/S; H.C. Andersens Boulevard 49, DK-1553 Copenhagen N (DK).


(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
10 March 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: TREATING CARTILAGE / BONE CONDITIONS WITH WATER-SOLUBLE STRONTIUM SALTS

(57) Abstract: Compounds and pharmaceutical compositions for use in the treatment and/or prophylaxis of cartilage and/or bone conditions and for methods of treating such condition. The compounds are salts of strontium that have a water-solubility of from about 1g/l to about 100g/l at room temperature, especially amino acid salts of strontium or dicarboxylic acid salts of strontium. Examples of novel water-soluble strontium salts are e.g. strontium glutamate and strontium alpha-ketoglutarate. The present invention also relates to an improved method for preparing the strontium salt of glutamic acid.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

<table>
<thead>
<tr>
<th>IPC</th>
<th>Classification Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>A61K33/24</td>
</tr>
<tr>
<td></td>
<td>A61P19/08</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>IPC</th>
<th>Classification Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>A61K</td>
</tr>
</tbody>
</table>

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

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

- EPO-Internal
- PAJ
- WPI Data
- BIOSIS
- EMBASE
- CHEM ABS Data

**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>EP 0 813 869 A (ADIR ET COMPAGNIE; LES LABORATOIRES SERVIER) 29 December 1997 (1997-12-29) page 2, line 29 - line 44 claim 1</td>
<td>1-7, 9-21, 24-34</td>
</tr>
<tr>
<td>A</td>
<td>SORBERA L A ET AL: &quot;STRONTIUM RANELATE TREATMENT AND PREVENTION OF OSTEOPOROSIS BONE RESORPTION INHIBITOR BONE FORMATION STIMULANT&quot; 1 April 2003 (2003-04-01), DRUGS OF THE FUTURE, BARCELONA, ES, PAGE(S) 328-335, XP008036784 ISSN: 0377-8282 abstract page 329, column 1, paragraph 3 - column 2, paragraph 1</td>
<td>1-34</td>
</tr>
</tbody>
</table>

**Further documents are listed in the continuation of box C.**

**Patent family members are listed in annex.**

* 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 document but published on or after the international filing data.
- **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.

- **T** 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.

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

27 January 2005

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

04/02/2005

**Name and mailing address of the ISA**

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk

Tel. (+31-70) 940-2040, Tx. 31 651 epo nl, Fax (+31-70) 940-3016

**Authorized officer**

Strack, E
<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>
</table>
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

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

   Although claims 24-31 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. \[ \square \] 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. \[ \square \] Claims Nos.: 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 additional sheet

1. \[ \square \] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. \[ \square \] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. \[ \checkmark \] 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.:

   1-22, 24-34 (partially); 23 (completely)

4. \[ \square \] 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.:

Remark on Protest

\[ \square \] The additional search fees were accompanied by the applicant's protest.

\[ \checkmark \] No protest accompanied the payment of additional search fees.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-22, 24-34 (partially), 23 (completely)
   Use of strontium glutamate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se, excluding strontium L-glutamate hexahydrate.

2. claims: 1-22, 24-34 (partially)
   Use of strontium aspartate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se excluding strontium L-aspartate trihydrate.

3. claims: 1-7, 9-21, 24-34 (partially)
   Use of strontium malonate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se.

4. claims: 1-7, 9-21, 24-34 (partially)
   Use of strontium maleate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se.

5. claims: 1-7, 9-21, 24-34 (partially)
   Use of strontium ascorbate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se.

6. claims: 1-22, 24-34 (partially)
   Use of strontium threonate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se.

7. claims: 1-7, 9-21, 24-34 (partially)
   Use of strontium lactate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se.

8. claims: 1-7, 9-21, 24-34 (partially)
Use of strontium pyruvate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se.

9. claims: 1-7, 9-21, 24-34 (partially)
Use of strontium alpha-ketoglutarate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se.

10. claims: 1-7, 9-21, 24-34 (partially)
Use of strontium succinate for the treatment/prophylaxis of any cartilage/bone disease/condition, pharmaceutical compositions thereof and the compound per se.

11. claims: 35, 36 (completely)
Preparation of strontium salts according to a process of claims 35 and 36
<table>
<thead>
<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
<th>Patent family member(s)</th>
<th>Publication date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AT 233558 T</td>
<td>15-03-2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AU 711950 B2</td>
<td>28-10-1999</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AU 2490297 A</td>
<td>08-01-1998</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BR 9703603 A</td>
<td>01-09-1998</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CA 2206837 A1</td>
<td>17-12-1997</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CN 1179944 A ,C</td>
<td>29-04-1998</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 69719408 D1</td>
<td>10-04-2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 69719408 T2</td>
<td>24-12-2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DK 813869 T3</td>
<td>02-06-2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 0813869 A1</td>
<td>29-12-1997</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ES 2193337 T3</td>
<td>01-11-2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HU 9701059 A2</td>
<td>02-03-1998</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 10059852 A</td>
<td>03-03-1998</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NO 972764 A</td>
<td>18-12-1997</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NZ 328106 A</td>
<td>27-04-2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 5856356 A</td>
<td>05-01-1999</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ZA 9705323 A</td>
<td>14-01-1998</td>
</tr>
</tbody>
</table>