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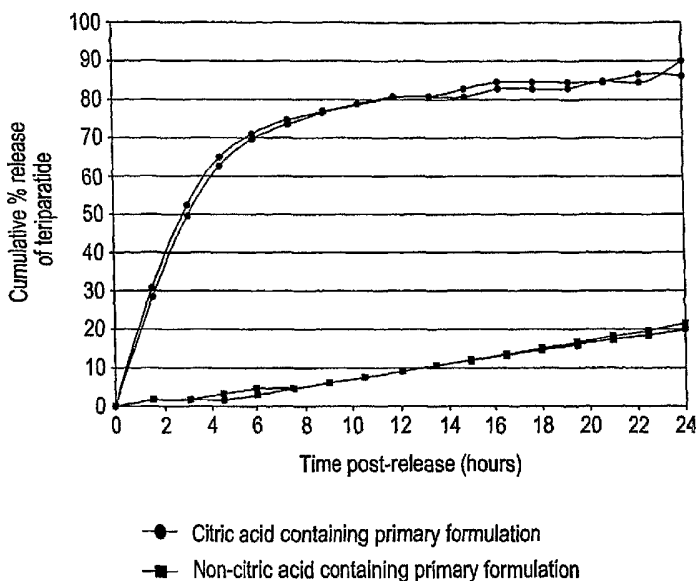
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(54) Title: CONTROL OF DRUG RELEASE BY TRANSIENT MODIFICATION OF LOCAL MICROENVIRONMENTS



(57) Abstract: Methods, formulations, and devices are provided for enhancing drug delivery from a medical device. The method is provided for increasing the rate or quantity of a drug formulation released from an implantable drug delivery device, which method comprises the step of providing a release-modifying agent within or proximate to the implantable drug delivery device, in a manner effective to inhibit gelation, aggregation, or precipitation of the drug formulation being released from the device. The drug formulation and the release-modifying agent may be stored together in at least one reservoir in the implantable drug delivery device. Alternatively, the release-modifying agent may be stored in one or more reservoirs separate from the drug formulation.

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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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.

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/002578

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61K38/29 A61K9/00 A61K47/12

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)
 A61K A61P

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 practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| X | US 2004/247671 A1 (PRESCOTT JAMES H ET AL) 9 December 2004 (2004-12-09) paragraph [0058] paragraph [0071] claims | 1-40 |
| X | US 2004/082937 A1 (AUSIELLO DENNIS ET AL) 29 April 2004 (2004-04-29) paragraph [0086] - paragraph [0087] claims | 1-40 |
| A | US 2004/265354 A1 (AMERI MAHMOUD ET AL) 30 December 2004 (2004-12-30) abstract example 2 claim 6 | 1-40 |
| | ----- -/-- | |

Further documents are listed in the continuation of Box C.

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
- *E* earlier document but published on or after the international filing date
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- *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

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International application No
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| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|---|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| A | US 5 496 801 A (HOLTHUIS ET AL) 5 March 1996 (1996-03-05) abstract claims ----- | 1-40 |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-40 (all in part)

Present independent claims 1 and 16 relate to methods/devices comprising compounds which has a given desired property or effect, namely "a release modifying agent". However, the description only provides support and disclosure in the sense of Article 6 and 5 PCT for very few such "release modifying agents". This non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of the claim (PCT Guidelines 9.19 and 9.20).

Also with regard to the unduly broad definition "drug", a restricted search had to be made.

With regard to the very large number of possible compounds falling under the definitions "drug" and "release modifying agent", the full search was restricted to the compounds specifically disclosed in the examples, namely citric or tartaric acid in combination with Teriparatide.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/002578

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

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.: 1-40 (all in part)
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:
see FURTHER INFORMATION sheet PCT/ISA/210

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

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

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 an additional fee, this Authority did not invite payment of any additional fee.

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.:

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.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/002578

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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