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(71) Applicant: SEPRACOR INC. [US/US]; 111 Locke
Drive, Marlborough, MA 01752 (US).

(72) Inventors: SENANAYAKE, Chrisantha, H.; 11 Old
Farm Circle, Shrewsbury, MA 01545 (US). RUBIN,
Paul, D.; 37 Greystone Lane, Sudbury, MA 01776 (US).
JERUSSI, Thomas, P.; 19 Garvey Road, Framingham,
MA 01701 (US).

(74) Agent: INSOGNA, Anthony, M.; Pennie & Edmonds
LLP, 1155 Avenue of the Americas, New York, NY 10036
(US).

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(54) Title: SYNTHESIS, METHODS OF USING, AND COMPOSITIONS OF HYDROXYLATED CYCLOBUTYLALKYLAMINES

(57) Abstract: The invention relates, in part, to making and using, and compositions comprising, racemic and stereomerically pure cyclobutylalkylamines, including hydroxylated sibutramine and hydroxylated metabolites of sibutramine. Methods of treating and preventing a variety of diseases and disorders are disclosed, as are pharmaceutical compositions and unit dosage forms that comprise compounds of the invention.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/47433

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C215/28 C07C215/42 C07C311/03 C07C311/04 C07C313/06
 C07C255/46 C07C47/46 A61K31/135 A61P25/24 C07F5/02

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)

IPC 7 C07C C07F 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, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 047 432 A (JOHN R. HOUSLEY ET AL) 10 September 1991 (1991-09-10) claims; example 64 --- -/--	1, 3, 6, 9, 13, 18, 21, 23-28, 32, 33, 35, 40, 44-59, 72, 73

 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 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

- *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

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20/09/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Zervas, B

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/47433

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>JEFFERY J E ET AL: "SYNTHESIS OF SIBUTRAMINE, A NOVEL CYCLOBUTYLALKYLAMINE USEFUL IN THE TREATMENT OF OBESITY, AND ITS MAJOR HUMAN METABOLITES" JOURNAL OF THE CHEMICAL SOCIETY, PERKIN TRANSACTIONS 1, CHEMICAL SOCIETY. LETCHWORTH, GB, no. 21, 1996, pages 2583-2589, XP000891897 ISSN: 0300-922X cited in the application page 2583, column 1, figure, compound 5a; page 2584, column 2, compound 13a; page 2587, column 2, paragraph 2 - page 2588, column 2, line 23</p>	1,4,5,7, 8,65
A	<p>--- WO 94 00047 A (SEPRACOR) 6 January 1994 (1994-01-06) cited in the application claims; examples</p>	1-4,9,32
A	<p>--- WO 94 00114 A (SEPRACOR) 6 January 1994 (1994-01-06) cited in the application claims; examples</p>	1-4,9,32
A	<p>--- US 4 746 680 A (JAMES E. JEFFERY ET AL.) 24 May 1988 (1988-05-24) cited in the application claims; examples -----</p>	1-4,9,32

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/47433

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:

Although claims 9 to 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. Claims Nos.: 1-43 (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 II Observations where unity of invention is lacking (Continuation of item 2 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-43 (all in part)

The scope of the claims 1 - 43, in as far as the expression "prodrug" is concerned, is so unclear (Article 6 PCT), that a meaningful International Search is impossible with regard to this expression.

The applicant's attention is drawn to the fact that claims, or parts of 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.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/47433

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International Application No

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