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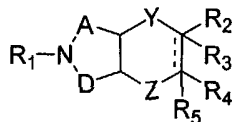
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*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*



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(54) Title: AZABICYCLIC COMPOUNDS ARE CENTRAL NERVOUS SYSTEM ACTIVE AGENTS



(I)

(57) Abstract: Compounds of formula (I), are novel CNS active agents that are useful for treating pain and for treating other disorders associated with the cholinergic system.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/25471

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	C07D401/04	C07D413/04	C07D417/04	C07D403/04	C07D471/04
	C07D495/04	C07D409/04	A61K31/4439	A61K31/422	A61K31/433
	A61K31/427	A61K31/4178	A61K31/437	A61K31/4365	A61K31/4025

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 C07D 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)

WPI Data, EPO-Internal, 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	WO 94 22823 A (ORTHO PHARMA CORP) 13 October 1994 (1994-10-13) claim 1; examples 1-9, 14, 15, 17-20, 22-25, 28-31, 35 ---	1,77
X	EFANGE ET AL: "Hydroxylated decahydroquinolines as ligands for the vesicular acetylcholine transporter: synthesis and biological evaluation" JOURNAL OF MEDICINAL CHEMISTRY., vol. 42, no. 15, 1999, pages 2862-2869, XP002270026 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623 page 2865, compounds 20 and 24 --- -/--	1,76,77

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
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- *&* document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 February 2004	01/03/2004
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 Alfaro Faus, I

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/25471

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/501 A61P25/00 A61P29/00 //(C07D471/04, 235:00, 221:00), (C07D495/04, 333:00, 221:00)

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)

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 929 087 A (EFANGE ET AL) 27 July 1999 (1999-07-27) claims 1,11; examples 5,6 -----	1,76,77
X	WO 95 17384 A (ORTHO PHARMA CORP) 29 June 1995 (1995-06-29) claim 1; examples, compounds 1-9, 14-17, 19 ----- -/--	1,77

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

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- *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.
- *Z* document member of the same patent family

Date of the actual completion of the international search

12 February 2004

Date of mailing of the international search report

Name and mailing address of the ISA

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Authorized officer

Alfaro Faus, I

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/25471

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KROW G R ET AL: "Synthesis of 5- and 6-(6-Chloro-3-pyridyl)-2-azabicyclo[2.2.0]hexanes. Epibatidine Analogs" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 56, no. 47, 17 November 2000 (2000-11-17), pages 9233-9239, XP004238580 ISSN: 0040-4020 table 3	1,76,77
X	EP 0 899 261 A (PFIZER) 3 March 1999 (1999-03-03) page 41, preparation 42, D	1
X	EP 0 612 741 A (THOMAE GMBH DR K) 31 August 1994 (1994-08-31) claims 1,8; examples 11-13	1,75
X	US 2002/094989 A1 (HALE ET AL) 18 July 2002 (2002-07-18) example 169 E and F	1
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/25471

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MARTIN ,S.F. ET AL: "Intramolecular '4+2' cycloadditions as a general strategy for alkaloid synthesis. A novel formal synthesis of lycorine" JOURNAL OF ORGANIC CHEMISTRY, vol. 47, no. 19, 1982, pages 3634-3643, XP002270027 AMERICAN CHEMICAL SOCIETY. EASTON., US ISSN: 0022-3263 compounds 21, 22 -----	1
X	EP 0 233 793 A (ROUSSEL UCLAF) 26 August 1987 (1987-08-26) example 1B -----	1
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P,X	WO 03 004493 A (NEUROSEARCH) 16 January 2003 (2003-01-16) page 8, lines 22-24 and 33-35; claim 1 and 32 -----	1,76,77

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1 - 81 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of formula I, where R2 or R4 is an heterocycle as shown in all the examples of the description and on page 4, lines 14 and 17; page 5, lines 7, 15, 20, 29 and following pages.

The scope of claims 1-81, in as far as the expression "amide, ester or prodrug thereof" 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 03/25471

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 76 - 81 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 compounds.
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:

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/25471

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Information on patent family members

International Application No

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INTERNATIONAL SEARCH REPORT

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