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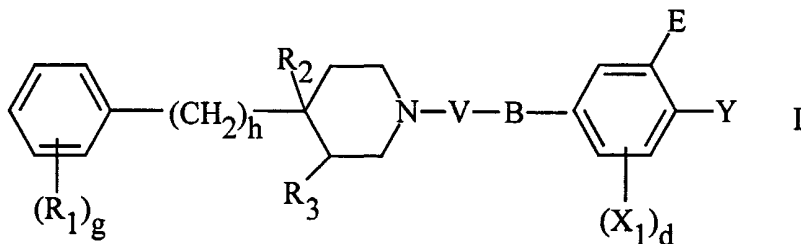
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(54) Title: PIPERIDINE DERIVATIVES AS SUBTYPE SELECTIVE N-METHYL-D-ASPARTATE ANTAGONISTS



(57) Abstract: Described are piperines of Formula (I) and pharmaceutically acceptable salts thereof. The compounds of Formula (I) are antagonists of NMDA receptor channel complexes useful for treating cerebral vascular disorders such as, for example, stroke, cerebral ischemia, central nervous system

disorders, depression, trauma, hypoglycemia, neurodegenerative disorders, anxiety, migraine headache, convulsions, Parkinson's disease, aminoglycoside antibiotics-induced hearing loss, psychosis, glaucoma, CMV retinitis, opioid tolerance or withdrawal, pain, especially chronic pain, neuropathic pain, or surgical pain, or urinary incontinence.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 01/02277

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C07D413/14 C07D417/14 A61K31/454 A61P9/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
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) CHEM ABS Data, EPO-Internal		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 12924 A (MERCK PATENT GMBH ;BARTOSZYK GERD (DE); PRUECHER HELMUT (DE); GOTT) 18 March 1999 (1999-03-18) page 1, line 1 - line 11 claims 1,4-10 page 2, line 23 - line 28 ---	1-15
X	EP 0 763 535 A (MERCK PATENT GMBH) 19 March 1997 (1997-03-19) claims 1,2,4-9 ---	1-15
X	WO 00 18763 A (CHEN XI ;HE XIAO SHU (US); NEUROGEN CORP (US)) 6 April 2000 (2000-04-06) page 4, line 14 -page 5, line 18 claims 30,31 Table 1, Compounds 5 & 6 ---	1-15
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<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> 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	Date of mailing of the international search report	
8 July 2002	25/07/2002	
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  Diedereren, J	

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/IB 01/02277

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>WO 96 16040 A (HORVATH RAYMOND F ;NEUROGEN CORP (US); PETERSON JOHN M (US); THURK) 30 May 1996 (1996-05-30) examples 16,17,18D page 6, line 7 - line 32</p>	1-15
X	<p>PRUECHER, H. ET AL: "(5S)-3-Aryl-5-(1-piperidinylmethyl)-2-oxazolidinones, a new class of potential neuroleptics with a high affinity for sigma receptors" BIOORG. MED. CHEM. LETT. (1992), 2(2), 165-70 , XP008005335 Compound 8r</p>	1-15
X	<p>WO 99 50264 A (KISHIBAYASHI NOBUYUKI ;KUMAZAWA TOSHIAKI (JP); SUZUKI KOJI (JP); I) 7 October 1999 (1999-10-07) -&amp; DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; Database accession no. 1999:640854 XP002205019 abstract</p>	1,4,12

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB 01/02277

## 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 14,15 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.:  
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.:  
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/IB 01/02277

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