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(54) Title: QUINOLINE DERIVATIVES AS NEUROKININ RECEPTOR ANTAGONISTS

(57) Abstract: The present invention relates to substituted quinoline-4-carboxylic acid hydrazides defined herein, pharmaceutical compositions comprising them and their use in treating diseases mediated by neurokinin-2 and/or neurokinin-3 (NK-3) receptors.

INTERNATIONAL SEARCH REPORT

Application No

PCT/GB2005/050120

A. CLASSIFICATION OF SUBJECT MATTER		
C07D215/52 A61K31/47 A61P25/18 C07D401/12 C07D417/12 C07D405/12 C07D409/12		
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) C07D		
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		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SAUDI, MANAL N. S. ET AL: "Synthesis of 2-(4-biphenyl)quinoline-4-carboxylate and carboxamide analogs. New human neurokinin -3 (hNK-3) receptor antagonists" ARCHIV DER PHARMAZIE (WEINHEIM, GERMANY) , 336(3), 165-174 CODEN: ARPMAS; ISSN: 0365-6233, 2003, XP009055980 examples 1,13b	1-37
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1955, XP002351596 retrieved from STN Database accession no. 1955:70743 abstract -/--	1,2, 8-13,32, 33
<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	
11 January 2006	02.02.2006	
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 Grassi, D	

INTERNATIONAL SEARCH REPORT

 Application No
 PCT/GB2005/050120

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	& JENEY, E.; ZSOLNAI, T.: "Experimental information on the chemotherapy of brucellosis" ACTA MICROBIOLOGICA ACADEMIAE SCIENTIARUM HUNGARICAE, vol. 2, 1955, pages 249-256, ----- DATABASE REGISTRY 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2001, XP002351597 retrieved from STN Database accession no. 349415-07-2 Compound: 349415-07-2 -----	1,2,9-13
X	 DATABASE REGISTRY 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2001, XP002351598 retrieved from STN Database accession no. 324063-32-3 Compound: 324063-32-3 abstract 	1,2,8-12
X	----- DATABASE REGISTRY 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2000, XP002351599 retrieved from STN Database accession no. 303067-46-1 Compound: 303067-46-1 abstract	1,2,8-12
Y	----- US 2003/236281 A1 (FARINA CARLO ET AL) 25 December 2003 (2003-12-25) ----- claims 1-10; examples 1-13	1,2, 5-20, 28-37
Y	----- WERMUTH ET AL: "The Practice of Medicinal Chemistry" PRACTICE OF MEDICINAL CHEMISTRY, 1996, pages 203-237, XP002190259 page 210	1,2, 5-20, 28-37
X	----- DATABASE ZREGISTRY 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 22 August 2003 (2003-08-22), XP002362091 retrieved from STN Database accession no. 571161-31-4 Compound: 571161-31-4 ----- ----- -/--	1,12,13

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INTERNATIONAL SEARCH REPORT

Application No
PCT/GB2005/050120

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE ZREGISTRY 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 12 August 2003 (2003-08-12), XP002362092 retrieved from STN Database accession no. 565174-86-9 Compound: 565174-86-9 -----	1,12,13
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002362093 retrieved from STN Database accession no. 1988:419527 Compounds: 115084-72-5, 115084-73-6 & VASIN, M. V. ET AL: "Radiomodifying efficiency of quinoline derivatives" RADIOBIOLOGIYA , 28(2), 274-6 CODEN: RADOA8; ISSN: 0033-8192, 1988, -----	1-4, 9-13, 21-24,26
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002362094 retrieved from STN Database accession no. 1989:147183 Compounds: 119778-67-5, 119778-68-6 & MOISEEV, I. K. ET AL: "Synthesis and antimicrobial activity of 4-substituted-2- cycloalkylquinolines" KHIMIKO-FARMATSEVTICHESKII ZHURNAL , 22(12), 1448-51 CODEN: KHfZAN; ISSN: 0023-1134, 1988, -----	1,9-13, 21
X	DATABASE ZREGISTRY 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 3 October 2000 (2000-10-03), XP002362095 retrieved from STN Database accession no. 292151-78-1 Compound: 292151-78-1 -----	1-4, 9-13, 21-24,26
X	DATABASE ZREGISTRY 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 14 August 2001 (2001-08-14), XP002362096 retrieved from STN Database accession no. 351328-07-9 Compound: 351328-07-9 ----- -/--	1,9-13, 21

INTERNATIONAL SEARCH REPORT

Application No
PCT/GB2005/050120

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	MONGA V ET AL: "Ring-substituted quinolines. Part 2: Synthesis and antimycobacterial activities of ring-substituted quinolinecarbohydrazide and ring-substituted quinolinecarboxamide analogues" BIOORGANIC & MEDICINAL CHEMISTRY, ELSEVIER SCIENCE LTD, GB, vol. 12, no. 24, 15 December 2004 (2004-12-15), pages 6465-6472, XP004646488 ISSN: 0968-0896 compounds 4B-D	1,9-13, 21
P,X	WO 2004/072045 A (MERCK SHARP & DOHME LIMITED; CHAMBERS, MARK, STUART; JONES, PHILIP; MA) 26 August 2004 (2004-08-26) cited in the application the whole document	1-37

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2005/050120

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.:
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 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:

see additional sheet

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.:
1-2(part), 3, 4, 5-13(part), 14-31, 32-37(part)
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

International Application No. PCT/GB2005/050120

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-2(part),5-13(part),14-20,28-30,31-37(part)

Compounds according to claim 1 in which R1 is optionally substituted phenyl.

2. claims: 1-2,5-13,32-37(all part)

Compounds according to claim 1 in which R1 is optionally substituted naphthyl.

3. claims: 1,5-13,31-37(all part)

Compounds according to claim 1 in which R1 is optionally substituted heteroaryl.

4. claims: 1,5-13,32-37(all part)

Compounds according to claim 1 in which R1 is ORa, SO2Ra, NRaRb or SO2NRaRb.

5. claims: 1,5-13,32-37(all part)

Compounds according to claim 1 in which R1 is C(O)Ra, COORa, CONRaRb.

6. claims: 1-2(part),3,4,5-13(part),31-37(part)

Compounds according to claim 1 in which R1 is an optionally substituted non-aromatic ring of 3-8 ring atoms.

INTERNATIONAL SEARCH REPORT

Information on patent family members

I Application No

PCT/GB2005/050120

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003236281 A1	25-12-2003	NONE	
WO 2004072045 A	26-08-2004	AU 2004210774 A1 CA 2514222 A1 EP 1594844 A1	26-08-2004 26-08-2004 16-11-2005