

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 October 2005 (27.10.2005)

PCT

(10) International Publication Number
WO 2005/100373 A3

(51) International Patent Classification:

C07H 9/04 (2006.01) A61K 31/7042 (2006.01)
C07H 15/00 (2006.01) A61P 37/00 (2006.01)
C07H 3/02 (2006.01) A61P 35/00 (2006.01)
A61K 31/70 (2006.01) A61P 17/00 (2006.01)
A61K 31/7028 (2006.01) A61P 11/06 (2006.01)

(21) International Application Number:

PCT/IB2005/000974

(22) International Filing Date: 13 April 2005 (13.04.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/561,791 13 April 2004 (13.04.2004) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
6 April 2006

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.

(54) Title: MONOSACCHARIDE DERIVATIVES AS ANTI-CANCER AND ANTI-INFLAMMATORY AGENTS

(57) Abstract: The present invention relates to monosaccharide derivatives as anti-inflammatory agents. The compounds disclosed herein can be useful for inhibition and prevention of inflammation and associated pathologies, including inflammatory and autoimmune diseases such as bronchial asthma, rheumatoid arthritis, type I diabetes, multiple sclerosis, allograft rejection, psoriasis, inflammatory bowel disease, ulcerative colitis, acne, atherosclerosis, cancer, pruritis or allergic rhinitis. Pharmacological compositions containing the compounds of the present invention and the methods of treating bronchial asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, multiple sclerosis, type I diabetes, psoriasis, allograft rejection, inflammatory bowel disease, ulcerative colitis, acne, atherosclerosis, cancer, pruritis or allergic rhinitis and other inflammatory and/or autoimmune disorders, using the compounds are also provided.

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A. CLASSIFICATION OF SUBJECT MATTER

C07H9/04 C07H15/00 C07H3/02 A61K31/70 A61K31/7028
 A61K31/7042 A61P37/00 A61P35/00 A61P17/00 A61P11/06

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)

C07H 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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94/11381 A (GREENWICH PHARMACEUTICALS INCORPORATED) 26 May 1994 (1994-05-26) cited in the application abstract	1-3, 7-23,31
X	US 5 298 494 A (ARORA ET AL) 29 March 1994 (1994-03-29) cited in the application abstract; claim 1	1-3, 7-23,31
X	WO 00/42053 A (RANBAXY LABORATORIES LIMITED; ARORA, SUDERSHAN, K; TANWAR, MADAN, P; G) 20 July 2000 (2000-07-20) abstract; claim 1	1-3, 7-23,31
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 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

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"O" document referring to an oral disclosure, use, exhibition or other means

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"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.

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Date of the actual completion of the international search

22 December 2005

Date of mailing of the international search report

20.01.06

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INTERNATIONAL SEARCH REPORT

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.
X	WO 94/28910 A (GREENWICH PHARMACEUTICALS INCORPORATED) 22 December 1994 (1994-12-22) cited in the application abstract; claim 1 -----	1-3, 7-23,31
P,X	WO 2004/071515 A (RANBAXY LABORATORIES LIMITED; SALMAN, MOHAMMAD; YADAV, GYAN, CHAND; SA) 26 August 2004 (2004-08-26) claims -----	1-3, 7-23,31
X	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1998, TOIKKA, MERJA ET AL: "Lignin-carbohydrate model compounds. Formation of lignin-methyl arabinoside and lignin-methyl galactoside benzyl ethers via quinone methide intermediates" XP002344213 retrieved from STN Database accession no. 130:139518 Compounds RN:220089-43-0 and RN:220089-44-1 abstract & JOURNAL OF THE CHEMICAL SOCIETY, PERKIN TRANSACTIONS 1: ORGANIC AND BIO-ORGANIC CHEMISTRY, (22), 3813-3818 CODEN: JCPRB4; ISSN: 0300-922X, 1998, -----	1
X	MASJOST B ET AL: "Structure based design, synthesis and in vitro evaluation of bisubstrate inhibitors for catechol O-methyltransferase (COMT)" CHEMISTRY - A EUROPEAN JOURNAL, VCH PUBLISHERS, US, vol. 6, no. 6, 2000, pages 971-982, XP002978173 ISSN: 0947-6539 page 975; compound 16 -----	1
X	WO 96/35431 A (CHEMORA PHARMOCHEM) 14 November 1996 (1996-11-14) claims -----	1
X	WO 93/13117 A (GREENWICH PHARMACEUTICALS INCORPORATED) 8 July 1993 (1993-07-08) abstract; claim 4 -----	1
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INTERNATIONAL SEARCH REPORT

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PCT/IB2005/000974

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 CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1985, PAULSEN, HANS ET AL: "Branched and chain-extended sugars, XXVIII. Synthesis of 6-amino-6-deoxyhepturonic acids" XP002360612 retrieved from STN Database accession no. 102:149685 Compound RN: 95580-78-2 abstract & LIEBIGS ANNALEN DER CHEMIE , (1), 113-28 CODEN: LACHDL; ISSN: 0170-2041, 1985, -----	1
X	COAT J.P. ET AL.: "Préparation et couplage sur des polypeptides de 5'-O-carboxyméthyl-ribonucléosides" CARBOHYDRATE RESEARCH, vol. 12, 1970, pages 335-346, XP002360609 Belgium compound 1 -----	1
P,X	KATIIYAR D ET AL: "Synthesis and antimycobacterial activities of glycosylated amino alcohols and amines" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 40, no. 4, April 2005 (2005-04), pages 351-360, XP004814470 ISSN: 0223-5234 table 1; compounds 15-23 -----	1
X	MISHRA, R. C. ET AL: "Synthesis of glycosylated .beta.-Amino hydroxamates as new class of antimalarials" BIOORGANIC & MEDICINAL CHEMISTRY , 11(24), 5363-5374 CODEN: BMECEP; ISSN: 0968-0896, 2003, XP002360610 tables 1,2; compounds 3-18 -----	1

INTERNATIONAL SEARCH REPORT

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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.:
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

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

1. claims: 1-3 (partly), 6 (compound 16), 7-23 (partly), 31

Compounds of formula I wherein XR5 represents A1)
-X-(CH₂)₂₋₄-ORe, the process for their preparation, a
pharmaceutical composition comprising them, and a
therapeutical method comprising their administration

2. claims: 1-2(partly), 7-23 (partly)

Compounds of formula I wherein XR5 is selected from A2)
-X-(CH₂)₂₋₄-NRj-C(O)ORs, A3) -X-(CH₂)₂₋₄-NRj-Y-Rd and A4)
-X-(CH₂)₂₋₄-NRj-C(=T)NRtRx, a pharmaceutical composition
comprising them, and a therapeutical method comprising their
administration

3. claims: 1-2 (partly), 4-5(partly), 6(compounds 13-15, 27),
7-23(partly), 27, 30

Compounds of formula I wherein XR5 represents A5) -X-
-(CH₂)₂₋₄-substituted heterocyclyl, the process for their
preparation, a pharmaceutical composition comprising them,
and a therapeutical method comprising their administration

4. claims: 1(partly), 3-5(partly), 6 (compounds 10, 22-25),
7-23(partly), 33, 34

Compounds of formula I wherein XR5 is selected from B1)
-X-(CH₂)₁₋₅-C(O)ORz, or B2) -X-(CH₂)₁₋₅-C(O)NRaRb, the
process for their preparation, a pharmaceutical composition
comprising them, and a therapeutical method comprising their
administration

5. claims: 1-23 (partly), 24-26, 27 (partly), 28-29, 32

Compounds of formula I wherein R1 is not hydrogen and XR5 is
(CH₂)₀₋₁-NRj-R5 and R5 is alkyl, alkenyl, alkynyl, aryl,
aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or
heterocyclalkyl, the process for their preparation, a
pharmaceutical composition comprising them, and a
therapeutical method comprising their administration

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB2005/000974

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9411381	A	26-05-1994	AU 5447894 A	08-06-1994
			CA 2149205 A1	26-05-1994
			CN 1091745 A	07-09-1994
			CN 1163270 A	29-10-1997
			DE 69312729 D1	04-09-1997
			DE 69312729 T2	04-12-1997
			EP 0668866 A1	30-08-1995
			IL 107427 A	12-03-1999
			JP 8506321 T	09-07-1996
			US 5432163 A	11-07-1995
			ZA 9308049 A	22-07-1994
US 5298494	A	29-03-1994	NONE	
WO 0042053	A	20-07-2000	AT 269349 T	15-07-2004
			AU 767948 B2	27-11-2003
			AU 1886000 A	01-08-2000
			BG 105795 A	31-05-2002
			BR 0007489 A	02-01-2002
			CA 2359980 A1	20-07-2000
			CN 1343212 A	03-04-2002
			CZ 20012541 A3	13-02-2002
			DE 60011568 D1	22-07-2004
			DE 60011568 T2	18-08-2005
			EP 1144425 A1	17-10-2001
			ES 2223447 T3	01-03-2005
			HK 1041006 A1	04-02-2005
			HR 20010527 A1	31-08-2002
			HU 0200097 A2	29-05-2002
			ID 30259 A	15-11-2001
			JP 2002534529 T	15-10-2002
			MA 25679 A1	01-04-2003
			NZ 512851 A	27-02-2004
			NZ 527482 A	25-02-2005
			PT 1144425 T	29-10-2004
SK 9962001 A3	05-02-2002			
TR 200102031 T2	21-12-2001			
WO 9428910	A	22-12-1994	AT 238804 T	15-05-2003
			AU 7101994 A	03-01-1995
			CA 2164827 A1	22-12-1994
			CN 1125398 A	26-06-1996
			DE 69432593 D1	05-06-2003
			DE 69432593 T2	27-11-2003
			EP 0715519 A1	12-06-1996
			JP 9501148 T	04-02-1997
			WO 2004071515	A
WO 9635431	A	14-11-1996	AU 5635496 A	29-11-1996
			US 5637570 A	10-06-1997
WO 9313117	A	08-07-1993	AT 163422 T	15-03-1998
			AU 3249593 A	28-07-1993
			CA 2104477 A1	21-06-1993
			CN 1077198 A	13-10-1993
			DE 69224520 D1	02-04-1998
			DE 69224520 T2	23-07-1998

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB2005/000974

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9313117	A	EP 0581916 A1	09-02-1994
		FI 933654 A	19-08-1993
		IL 104112 A	30-09-1997
		JP 6508152 T	14-09-1994
		NZ 246305 A	28-10-1996
