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WO 2004/005310 A3

(54) Title: NEW COMPOUNDS, COMPOSITIONS AND METHODS FOR TREATMENT OF INFLAMMATORY DISEASES AND CONDITIONS



(I)

(57) Abstract: The present invention relates (a) to new compounds represented by Formula (I): wherein M represents a macrolide subunit (macrolide moiety) derived from macrolide possessing the property of accumulation in inflammatory cells, S represents a steroid subunit (steroid moiety) derived from steroid drug with anti-inflammatory activity and L represents a linker molecule linking M and S, (b) to their pharmacologically acceptable salts, prodrugs and solvates, (c) to processes and intermediates for their preparation, and (d) to their use in the treatment of inflammatory diseases and conditions in humans and animals. Such compounds inhibit many cytokines and immune mediators involved in immune responses which cause inflammation, allergy, or alloimmunity, including without limitation IL-1, 2, 4, 5, 6, 10, 12, GMCSF, ICAM, and TNF-α. Importantly, anti-inflammatory steroids exert a direct anti-inflammatory effect through binding to the glucocorticosteroid receptor.

INTERNATIONAL SEARCH REPORT

Internat ɔlication No
PCT/HR 03/00037

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07J43/00 C07H17/00 C07H17/08 A61K31/58 A61P5/44

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 C07J 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, WPI 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.
A	ROMO D ET AL: "Total Synthesis and Immunosuppressive Activity of (-)-Pateamine A and Related Compounds: Implementation of beta-Lactam Based MacroCYCLIZATION" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, US, vol. 120, no. 47, 1998, pages 12237-12254, XP002200620 ISSN: 0002-7863 compound 69 abstract ---	1,50
A	WO 97 41255 A (MASSACHUSETTS INST TECHNOLOGY) 6 November 1997 (1997-11-06) figures --- -/--	1,50

[X] Further documents are listed in the continuation of box C.

[X] 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 February 2004	27/02/2004

Name and mailing address of the ISA	Authorized officer
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	de Nooy, A

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Internati plication No
PCT/HR 03/00037

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 64040 A (ADVANCED MEDICINE INC ;GRIFFIN JOHN H (US); JUDICE J KEVIN (US)) 16 December 1999 (1999-12-16) page 68 line 24-page 69 line 8 figures	1,50
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A	BRANDT-RAUF P ET AL: "FLUORESCENT ASSAY FOR ESTIMATING THE BINDING OF ERYTHROMYCIN DERIVATIVES TO RIBOSOMES" ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, DC, US, vol. 14, no. 1, July 1978 (1978-07), pages 88-94, XP000923144 ISSN: 0066-4804 compound 61	1
P,X	WO 02 055531 A (HRVACIC BOSKA ;MESIC MILAN (HR); PLIVA D D (HR); KOMAC MARIJANA (H) 18 July 2002 (2002-07-18) the whole document	1-54

INTERNATIONAL SEARCH REPORT

International application No.
PCT/HR 03/00037

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:

2. ☒ Claims Nos.: 1, 3-4, 7, 48-54 (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, 3-4, 7, 48-54 (all in part)

Present claims 1, 3-4, 7, 48-54 relate to an extremely large number of possible compounds. In fact, the claims contain so many options that a lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear, namely those parts relating to compounds of claim 1 of Formula I where M represents a group of Formula II of claim 2.

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

Information on patent family members

Internatic pplication No
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