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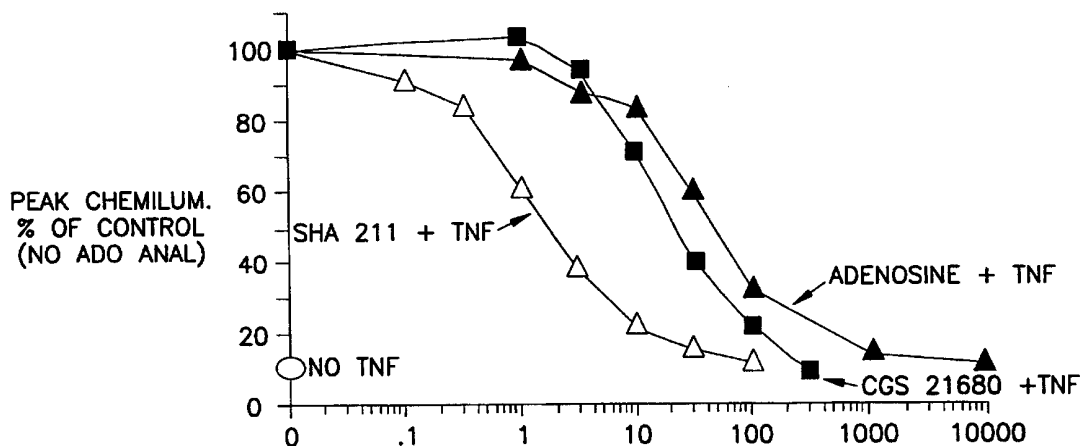
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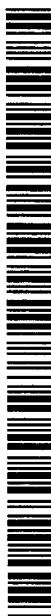
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09/320,769 27 May 1999 (27.05.1999) US
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(54) Title: METHOD AND COMPOSITIONS FOR TREATING THE INFLAMMATORY RESPONSE



(57) Abstract: Agonists of A_{2A} adenosine receptors optionally, in combination with a Type IV phosphodiesterase (PDE) inhibitor are effective for the treatment of the inflammatory response of mammalian tissue.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/14548

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/00 A61K31/7076 A61P29/00 //(A61K31/7076,31:4015)

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 A61K

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	US 5 877 180 A (LINDEN JOEL M ET AL) 2 March 1999 (1999-03-02) see the whole document, especially column 7 lines 36-column 8; column 9 line 13; column 11 lines 36-39; column 13 lines 5-28; column 14 lines 34-37 ---	1-10
X	SULLIVAN ET AL.: "Role of A2a adenosine receptors in inflammation" DRUG DEVELOPMENT RESEARCH, vol. 45, no. 3-4, 1998, pages 103-112, XP000978332 see the whole document, especially page 106 right column and page 109 left column last paragraph --- -/--	1-10

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
- *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

24 January 2001

Date of mailing of the international search report

01/02/2001

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/14548

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>BUSTER B(A) ET AL: "The effect of adenosine receptor agonists on neutrophil pleocytosis and blood-brain barrier pathophysiology in experimental bacterial meningitis" ABSTRACTS OF THE INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, XX, XX, vol. 37, 1997, page 39 XP002104913 see abstract B-72</p> <p style="text-align: center;">---</p>	1-6,8-10
X	<p>WO 98 57651 A (MCAFEE DONALD A ;DISCOVERY THERAPEUTICS INC (US); MARTIN PAULINE L) 23 December 1998 (1998-12-23) abstract page 2 see page 3 especially lines 17-18 page 8, line 23 - line 29 see page 9 lines 1-18, especially lines 2,3,8-10 page 11, line 3 - line 23 page 12, line 2 - line 3 claims 10,11</p>	1,3,4,7,8
Y	<p style="text-align: center;">---</p>	2,5,9,10
Y	<p>SULLIVAN GW ET AL: "The specific type IV phosphodiesterase inhibitor rolipram combined with adenosine reduces tumor necrosis factor-alpha-primed neutrophil oxidative activity" INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, US, ELMSFORD, NY, vol. 17, no. 10, 1995, pages 793-803, XP002104914 ISSN: 0192-0561 the whole document</p> <p style="text-align: center;">---</p>	2,5,9,10
P,X	<p>WO 99 34804 A (UNIV VIRGINIA) 15 July 1999 (1999-07-15) the whole document</p> <p style="text-align: center;">---</p>	1-10
P,X	<p>SULLIVAN ET AL.: "Neutrophil A2a adenosine receptor inhibits inflammation in a rat model of meningitis: synergy with type IV phosphodiesterase inhibitor, Rolipram" JOURNAL OF INFECTIOUS DISEASES, vol. 180, no. 5, November 1999 (1999-11), pages 1550-1560, XP000978330 the whole document</p> <p style="text-align: center;">-----</p>	1-6,8-10

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 3 and 5 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 (only for rolipram and compounds of claim 4). 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.

Moreover, present claims 1,2,9,10 relate to compounds and methods defined by reference to a desirable property, namely being and "agonist of an A2a adenosine receptor" or a "type IV phosphodiesterase inhibitor". The claims cover all compounds/methods property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds (or methods). 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. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound or a method by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds (or methods) of claims 4 and/or 6.

Therefore the search has been carried out :

- incompletely on claims 1-3, 5-10
- completely on claim 4 .

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

International Application No

PCT/US 00/14548

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5877180	A	02-03-1999	NONE	
WO 9857651	A	23-12-1998	AU 8074098 A EP 1014995 A	04-01-1999 05-07-2000
WO 9934804	A	15-07-1999	AU 2108299 A EP 1044004 A	26-07-1999 18-10-2000