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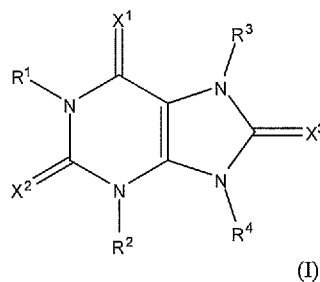
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(54) Title: DERIVATIVES OF URIC AND THIOURIC ACID FOR OXIDATIVE STRESS-RELATED DISEASES



(57) Abstract: Disclosed is a method of treating or preventing an oxidative stress-related disease in a mammal in need thereof comprising administering an effective amount of a compound of formula (I) to the mammal, wherein R^1 - R^4 and X^1 - X^3 are as described herein. Examples of the oxidative stress-related diseases are a neurological disorder, a cardiovascular disorder, and a wound.

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/076597

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K31/52 A61K31/522 A61P17/02 A61P25/00

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)

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, BIOSIS, EMBASE, 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 2006/024545 A (STICHTING TECH WETENSCHAPP [NL]; HAGEMAN GERRIGJE JOHANNA [NL]; MOONEN) 9 March 2006 (2006-03-09) page 1, line 29 - line 31 page 2, line 7 - line 23 page 15, line 3 - line 30 page 19, line 1 - line 9 -----	1-6,8, 10,11, 15,16
X	US 6 878 715 B1 (KLEIN J PETER [US] ET AL) 12 April 2005 (2005-04-12) column 185 - column 186; table 2; compound CT11499 column 6, line 35 - line 56 ----- -/-	1-5,8, 10,16

☒ Further documents are listed in the continuation of Box C.☒ See patent family 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
- *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

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* & * document member of the same patent family

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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 96/20710 A (UNIV CALIFORNIA [US]) 11 July 1996 (1996-07-11) page 9; table I; compounds 24,25 page 14; compounds 24,25 page 1, line 10 - line 16 page 3, line 11 - line 19 -----	1,2,5,8, 10-12,16
X	WO 00/00491 A (UNIV CALIFORNIA [US]) 6 January 2000 (2000-01-06) page 39; compounds 24,25 page 64, line 11 - line 16 table 2; compounds 24,25 page 62, line 1 - line 10 -----	1,2,8, 10-12,16
Y	YU Z F ET AL: "Uric acid protects neurons against excitotoxic and metabolic insults in cell culture, and against focal ischemic brain injury in vivo." JOURNAL OF NEUROSCIENCE RESEARCH 1 SEP 1998, vol. 53, no. 5, 1 September 1998 (1998-09-01), pages 613-625, XP002495617 ISSN: 0360-4012 abstract page 613, column 2, paragraph 2 page 617, column 2, paragraph 2 - paragraph 3 page 621; figure 6 -----	13,14
Y	BHAT V B ET AL: "Efficient scavenging of hydroxyl radicals and inhibition of lipid peroxidation by novel analogues of 1,3,7-trimethyluric acid." LIFE SCIENCES 14 DEC 2001, vol. 70, no. 4, 14 December 2001 (2001-12-14), pages 381-393, XP002495618 ISSN: 0024-3205 page 382, paragraph 1 page 383; table 1 page 385, paragraph 4 - paragraph 5 page 386; table 2 page 387; figure 1; table 3 page 388 page 390, paragraph 1 page 391, paragraph 3 -----	13,14

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/076597

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JANARDHAN V ET AL: "Mechanisms of ischemic brain injury" CURRENT CARDIOLOGY REPORTS, CURRENT SCIENCE, PHILADELPHIA, PA, US, vol. 6, no. 2, 1 March 2004 (2004-03-01), pages 117-123, XP008096241 ISSN: 1523-3782 page 117, column 1, paragraph 1 page 118; figure 1 -----	
A	NISHIDA Y: "INHIBITION OF LIPID PEROXIDATION BY METHYLATED ANALOGUES OF URIC ACID" JOURNAL OF PHARMACY AND PHARMACOLOGY, vol. 43, no. 12, 1991, pages 885-887, XP008096421 ISSN: 0022-3573 page 885, column 1, paragraph 1 page 885, column 2; table 1 page 886 -----	
A	DJALDETTI RUTH ET AL: "Neuroprotection in progressive brain disorders." THE ISRAEL MEDICAL ASSOCIATION JOURNAL : IMAJ AUG 2003, vol. 5, no. 8, August 2003 (2003-08), pages 576-580, XP002495619 ISSN: 1565-1088 page 576, column 2, paragraph 2 page 577, column 1 -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/076597

Box No. 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 No. 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 allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers 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.:

see annex

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

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

1. claims: 1-4, 10-16 in part and claims 5, 6, 8 completely

Use of a compound of formula I for the treatment/prevention of a oxidative stress-related disease which is a neurological disorder, in particular ischemic brain injury, trauma, epilepsy, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, tauopathy and dementia.

2. claims: 1-4, 10-16 in part

Use of a compound of formula I for the treatment/prevention of a oxidative stress-related disease which is arthritis.

3. claims: 1-4, 10-16 in part

Use of a compound of formula I for the treatment/prevention of a oxidative stress-related disease which is respiratory distress.

4. claims: 1-4, 10-16 in part

Use of a compound of formula I for the treatment/prevention of a oxidative stress-related disease which is retinal degeneration.

5. claims: 1, 10-16 in part and claims 7, 9 completely

Use of a compound of formula I for the treatment/prevention of a oxidative stress-related disease which is a wound or for enhancing wound healing.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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