(54) Title: CASPASE-1 INHIBITORS AND METHODS FOR THEIR USE

(57) Abstract: The invention provides compounds of Formula I and derivatives thereof, pharmaceutical compositions comprising a compound of Formula I, and methods of treatment utilizing such compounds and compositions: wherein: R1 chosen from optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl; L is a linker; R2 is chosen from optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl; and Y is or single stereoisomers, mixtures of stereoisomers, or the pharmaceutically acceptable salts, amides, or esters thereof.

![Chemical Structure](image-url)
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.
INTERNATIONAL SEARCH REPORT

INTERNATIONAL APPLICATION No.
PCT/US03/18021

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61K 38/05; C07K 5/06
US CL. : 514/19; 549/76
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)
U.S. : 514/19; 549/76

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)
CAS online

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>P,X</td>
<td>US 6,566,338 A (WEBER et al) 20 May 2003(20.05.2003, column 12 lines 16+, column 9 lines 45+, column 10 lines 1-70.</td>
<td>1-3, 12, 20-21 and 27</td>
</tr>
</tbody>
</table>

☐ 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 application or patent 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

"+" 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
"Å*" document member of the same patent family

Date of the actual completion of the international search: 15 December 2003 (15.12.2003)
Date of mailing of the international search report: 27 MAY 2004

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Form PCT/ISA/210 (second sheet) (July 1998)
Continuation of Box 1 Reason 2:
In these claims, the numerous variables (e.g., R1, R2, L, Y etc.) and their voluminous complex meanings and their seemingly endless permutations and combinatoric and the lengthy list of named compounds in claim 20, along with the numerous methods of use involved make it virtually impossible to determine the full scope and complete meaning to the claimed subject matter. As presented, the subject matter cannot be regarded as being a clear and concise description for which protection is sought and as such the listed claims do not comply with the requirements of PCT Article 6. Thus it is impossible to carry out a meaningful search on the same. A search will be made on the first discernable invention of claim 20 which is the compound, N-(2,3-bis(4-chlorophenyl)-1-methylpropyl)-1,4-benzodiaxone-2-carboxamide, listed in claim 15 and related claim 21.
INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [ ] Claim Nos.:因为 they relate to subject matter not required to be searched by this Authority, namely:

2. [ ] Claim Nos.:因为 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:
   Please See Continuation Sheet

3. [ ] Claim Nos.: 4-11,14-19,22-26 and 28因为 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.

Form PCT/ISA/210 (continuation of first sheet(1)) (July 1998)