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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: DIHETERO-SUBSTITUTED METALLOPROTEASE INHIBITORS

(57) Abstract: Disclosed are compounds which are inhibitors of metalloproteases and which are effective in treating conditions characterized by excess activity of these enzymes. In particular, the compounds have a structure according to formula (I): where J, M, Q, T, W, X, Z, R¹, R², R³, R⁴, R⁵, R⁶, R^{6'}, R⁷, m, and n have the meanings described in the specification. This invention also includes optical isomers, diastereomers and enantiomers of the formula above, and pharmaceutically-acceptable salts, biohydrolyzable amides, esters, and imides thereof. Also disclosed are pharmaceutical compositions comprising these compounds, and methods of treating or preventing metalloprotease-related maladies using the compounds or the pharmaceutical compositions.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/05195

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D277/36 C07C311/19 C07D249/12 A61K31/41 A61K31/426
C07D233/84 C07D235/28 C07D239/95 C07D277/74 A61K31/428
C07D263/58 C07D257/04 A61K31/433 C07D285/125 C07D333/34

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 C07D C07C 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)

CHEM ABS Data, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 06340 A (PROCTER & GAMBLE) 11 February 1999 (1999-02-11) see whole document, especially the examples and formula I ---	1-16
A	WO 98 08822 A (PROCTER & GAMBLE) 5 March 1998 (1998-03-05) the whole document --- -/--	1-16



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

15 September 2000

Date of mailing of the international search report

28.09.00

Name and mailing address of the ISA

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Scruton-Evans, I

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/05195

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D271/113 C07D413/04 C07D307/64 C07D239/38 C07D213/70
C07D487/04 C07D311/16 A61K31/4402 A61K31/4406 A61K31/44
A61P19/02 A61P35/04 A61P9/00 C07D319/04 C07D339/08

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P, A	DE B ET AL: "The next generation of MMP inhibitors: design and synthesis" ANN. N. Y. ACAD. SCI. (ANYAA9,00778923);1999; VOL.878 (INHIBITION OF MATRIX METALLOPROTEINASES); PP.40-60, XP000916382 Procter & Gamble Pharmaceuticals;Mason; 45040-8006; OH; USA (US) the whole document --- -/--	1-16

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Scruton-Evans, I

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Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, A	CHENG M ET AL: "Design, Synthesis, and Biological Evaluation of Matrix Metalloproteinase Inhibitors Derived from a Modified Proline Scaffold" J. MED. CHEM. (JMCMAR, 00222623); 1999; VOL. 42 (26); PP. 5426-5436, XP000919157 Procter and Gamble Pharmaceuticals; Mason; 45040; OH; USA (US) the whole document -----	1-16

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- "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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Scruton-Evans, I

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/05195

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:

Although claims 14-16 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1-11 (partly)
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.: 1-11 (partly)

Present claims 1-11 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. 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. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds wherein W is CH=CH and X is OH, with J as OH or R15 and R13 together as a cyclic C(X)(X) derivative (as in examples 68-72) i.e. all of the examples and closely related homologous compounds.

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 00/05195

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9906340 A	11-02-1999	AU 8237698 A EP 1009737 A NO 20000464 A ZA 9806835 A	22-02-1999 21-06-2000 30-03-2000 01-02-1999
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