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PCT/MIA/VI/14

ORIGINAL: English

DATE: February 11, 1997

WORLD INTELLECTUAL PROPERTY ORGANIZATION
GENEVA

**INTERNATIONAL PATENT COOPERATION UNION
(PCT UNION)**

**MEETING OF INTERNATIONAL AUTHORITIES
UNDER THE PCT**

**Sixth Session
Canberra, February 17 to 21, 1997**

RESTRICTIONS OF INTERNATIONAL SEARCH FOR REASONS OF ECONOMY

Proposal by the European Patent Office

The Annex to this document contains proposals by the European Patent Office concerning possible restrictions of international search for reasons of economy where international applications claim extremely broad, vague or imprecisely formulated claims, submitted for consideration at the sixth session of the Meeting of International Authorities under the PCT.

[Annex follows]

EUROPEAN PATENT OFFICE

5 February 1997

RESTRICTED SEARCH FOR ECONOMICAL REASONS

I. Problem

1. The EPO would like to submit for discussion at the MIA/VI meeting the following problem relating to the incompleteness of the international search in certain situations.
2. In chemistry, but it also happens in other technical fields, applicants tend more and more to draft very broad claims. Two categories at least of such broad claims may occur :
 - a) Extremely broad Markusch-type claims (see Annex 1);
 - b) Other extremely broad, vague or imprecisely formulated claims (see Annex 2). As a rule such claims are not even substantiated by a sufficient number of examples.

This means that to carry out a search reasonably completely, i.e. as in usual case and within an average time of 1 to 1.5 days, a search examiner would need eg. 30 days or even more for the search.

3. Rule 33.3(b) PCT provides that the ISA should cover the entire subject matter of the claims **in so far as possible and reasonable**. Furthermore, the PCT Guidelines for search, Chapter III-3.6 and III-3.7 give additional clarification on how to interpret Rule 33.3(b) and refer explicitly to **reasons of economy or unduly wide or speculative claims** that may allow an ISA to restrict the search effort.

In the case of Annexes 1 and 2, the last sheet called Annex 1a and 2a show wordings which have been used to indicate in the ISR the restrictions brought to the search.

4. The EPO would like to know whether other ISAs face similar problems.

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II. Formal aspect

5. Form PCT/ISA/210, Box I of Continuation of first sheet covers the case of incomplete search of certain claims because they do not comply with the requirements of the PCT to such an extent that no meaningful search can be carried out. Box I currently refers generally to Art. 17(2)(a) PCT so that it is not specifically appropriate to cope with the situation that has been explained above. However the EPO has felt in clear-cut cases obliged to use that existing Box, as it may be seen from Annexes 1a and 2a.
 6. Therefore the EPO is of the view that Box 1 would gain in clarity if it would be amended as indicated in Annex 3.
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ANNEX 1

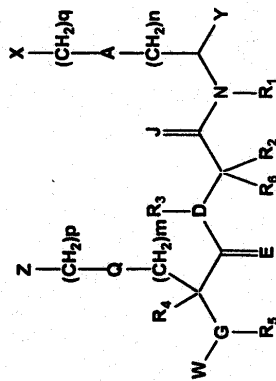
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5 WHAT IS CLAIMED IS:

1. A compound represented by the formula:



10 wherein:

m = 0,1,2,3,4;

n = 0,1,2,3,4;

p = 0,1,2,3,4;

q = 0,1,2,3,4;

15 Y = CHO, COCF₃, COCF₂CF₃, COCO₂R₇, COCONR₈R₉, B(OR)₁₀;

where: R₇, R₈, R₉, R₁₀ are the same or different and = H, C₁-

alkyl, C₃-cycloalkyl, aryl, C₁-3alkyl, heteroaryl, C₁-3alkyl;

A = piperidinyl, pyrrolidinyl, cyclopropyl, cyclobutyl, cyclopentyl,

cyclohexyl, phenyl, C₃-heteroaryl, or is absent;

20 R₁ = H or C₁-3alkyl;

J = O or H₂;

R₂ = H or C₁-3alkyl;

D = N, CH, NCH₂, NCH₂CH₂, CHCH₂;

R₃ = H or C₁-3alkyl;

E = O or H₂;

R₄ = H or CH₃;

Q = piperidinyl, pyrrolidinyl, C₃-8 cycloalkyl, phenyl, substituted phenyl,

naphthyl, pyridyl, or is absent;

G = N, CH, or is H;

R₅ = H or C₁-3 alkyl, or is absent if G is H;

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5 R₆ = H or CH₃;

W = H, arylacyl, heteroarylacyl, aryl(C₁-3alkyl)sulfonyl, arylsulfonyl,

substituted arylsulfonyl, aryl(C₁-4alkenyl)sulfonyl, C₁-8 alkylsulfonyl,

heteroaryl(C₁-3alkyl)sulfonyl, heteroarylsulfonyl, aryloxy carbonyl, C₁-6

alkyloxy carbonyl, aryl(C₁-3alkyloxy) carbonyl, arylaminocarbonyl, C₁-

alkylaminocarbonyl, aryl(C₁-3alkyl)aminocarbonyl, HOOC-C₀-

3alkyl carbonyl, or is absent if G is H;

X = H, C₁-alkyl, NR₁R₂, NH-C(NR₁R₂)=NH, NH-C(NHR₁)=NR₂, S-

C(NR₁R₂)=NH, S-C(NHR₁)=NR₂, C(NR₁R₂)=NH, C(NHR₁)=NR₂, or

CR₁=NR₂; where: R₁, R₂ are the same or different and = H, C₁-6alkyl,

C₁-3aryalkyl, aryl or where R₁R₂ forms a cyclic ring containing

(CH₂)_p where p=2-5, with the proviso that when X is H or C₁-alkyl,

then A must contain at least one N atom;

Z = H, C₁-alkyl, NR₁R₂, NH-C(NR₁R₂)=NH, NH-C(NHR₁)=NR₂, S-

C(NR₁R₂)=NH, S-C(NHR₁)=NR₂, C(NR₁R₂)=NH, C(NHR₁)=NR₂, or

CR₁=NR₂; where: R₁, R₂ are the same or different and = H, C₁-6alkyl,

C₁-3aryalkyl, aryl or where R₁R₂ forms a cyclic ring containing

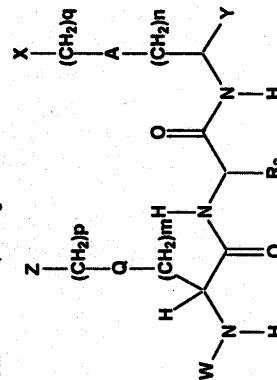
(CH₂)_p where p=2-5, with the proviso that when Z is H or C₁-alkyl,

then Q must contain at least one N atom;

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrg

25 derivatives thereof.

2. The compound of claim 1, having the formula:



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3. The compound of claim 1, having an IC50 for Factor Xa of less than about 200 nM.

4. The compound of claim 1, having an IC50 for prothrombinase of less than about 2.0 µM.

5. The compound of claim 1, having an IC50 for thrombin of greater than about 1.0 µM.

6. A compound selected from a group consisting of:

- 15 H-D-Arg-Gly-Arg-H
- Boc-D-Arg-Gly-Arg-H
- HOCCCO-D-Arg-Gly-Arg-H
- HOCCCH2CO-D-Arg-Gly-Arg-H
- HOOC(CH2)2CO-D-Arg-Gly-Arg-H
- PhCH2CH2CO-D-Arg-Gly-Arg-H
- PhCH2SO2-D-Arg-Gly-Arg-H
- EtOCCO-D-Arg-Gly-Arg-H
- 2-NaphthoxyAc-D-Arg-Gly-Arg-H
- Boc-D-Cit-Gly-Arg-H
- Boc-D-Lys-Gly-Arg-H
- Boc-D-Har-Gly-Arg-H
- Boc-D-Har((CH3)4)-Gly-Arg-H
- Boc-D-Arg-Ala-Arg-H
- Boc-D-Arg-D-Ala-Arg-H
- Boc-D-Arg-β-Ala-Arg-H
- Boc-D-Arg-Alb-Arg-H
- Boc-D-(2,3-Dap)-Gly-Arg-H
- Boc-D-(2,4-Dab)-Gly-Arg-H
- γ-Abu-Gly-Arg-H
- Boc-D-Om-Gly-Arg-H
- Boc-D-homoLys-Gly-Arg-H
- Boc-Bag-Gly-Arg-H
- Boc-D-4-Gpa-Gly-Arg-H

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INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 96/ 09285

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

Remark : As the general formula of claim 1 contains no fixed invariable elements, a complete search was considered not to be possible for economical reasons. The searched subject matter includes all the compounds of claim 6 ; this claim includes all the real examples.

Claims completely searched : 6
Claims incompletely searched : 1-5, 7-10

Remark : Although claim 7-10 refer to a method of treatment, the search was carried out and based on the alleged effects of the compounds.

ANNEX 2

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Claims

1. A novel compound which has cysteinyl protease inhibitor activity and is capable of inhibiting proteolytic cleavage of membrane bound CD23 in vivo excluding L-trans-epoxysuccinyl-leucylamido (4-guanidino) butane (E64).
2. A compound according to claim 1 which is a substrate for Der p I and is selected from the group consisting of: E64 analogues, peptidomimetics and mimetics thereof.
3. A compound according to claim 1 which is selected from the group consisting of : peptide sequences and analogues and mimetics thereof comprising cleavage site(s) which is/are capable of being cleaved by Der p I.
4. A cysteinyl protease inhibitor compound which includes a chemical composition capable of adopting a structure essentially equivalent to an inhibitor of the enzyme Der p I, excluding E64, optionally together with a pharmaceutically acceptable carrier or excipient for use in the treatment of allergic diseases.
5. A cysteinyl protease inhibitor compound capable of adopting a structure having a pharmacophoric pattern essentially equivalent to the pharmacophoric pattern of a section of an inhibitor of Der p I, excluding E64.

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43. Use of a compound or ligand according to any one of claims 1 to 23 in the manufacture of a medicament for the treatment of allergic diseases including juvenile asthma and eczema.

44. Use of a pharmaceutical composition according to claim 36 in the manufacture of a medicament for the treatment of allergic diseases including juvenile asthma and eczema.

45. Use of a compound or ligand according to any one of claims 1 to 23 for the manufacture of a medicament for prophylactic prevention of allergic diseases including juvenile asthma and eczema.

46. Use of a pharmaceutical composition according to claim 36 for the manufacture of a medicament for prophylactic prevention of allergic diseases including juvenile asthma and eczema.

47. A cysteinyl protease inhibitor compound selected from the group which consists of:

- Compound 1: N-Benzoyl-L-valyl-L-alanyl-L-norleucine
- Compound 2: N-Benzoyl-L-valyl-L-alanyl-L-norleucine bromomethyl ketone
- Compound 3: N-Benzoyl-L-valyl-L-alanyl-L-norleucine 2,6-bis (trifluoromethyl) benzoyloxy methyl ketone
- Compound 4: N-Benzoyl-L-valyl-L-alanyl-L-norleucine 2,6-dimethyl benzoyloxy methyl ketone

INTERNATIONAL SEARCH REPORT

International Application No. PCT/GB 96/ 01707

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

Remark :

The claims of the present application are formulated in a very vague and imprecise manner. The claimed subject matter would seem to refer, according to claim 1, to any irreversible cysteine protease inhibitor with a unique exception (E64), in the opinion of the Search Division this makes a complete search impossible for economical reasons. Guided by the description, the search has been limited to the compounds of claim 47, which includes all the real examples as well as some intermediates. Compounds 17-22, which are claimed as their preparation, which is contradictory with the definition of the claimed subject matter, were searched as compounds per se. Compound 33 of claim 47 has been searched as if it were reading "Ethyl-(S)-(E)-3-(Morpholinoyl amino-L-valyl-L-alanyl-) amino-6-methyl-hept-2-enoate, the last part of the name having obviously slipped away.

Claims incompletely searched: 1-46, 48
Claim completely searched: 47

Remark: Although claims 27-29, 31-32 (at least partially), 33, 39-42 refer to a method of treatment of the human body, the search was carried out and based on the alleged effects of the compounds.

ANNEX 3

INTERNATIONAL SEARCH REPORT

International application No.

Box I - Observations where certain claims were found unsearchable or incompletely searchable (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) and (b) for the following reasons:

1. Claims Nos.:

These claims relate to subject matter not required to be searched by this Authority (Art. 17(2)(a)(i) and Rule 39.1), namely :

2. Claims Nos.:

These claims do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out because the claims contain obscurities, inconsistencies or contradictions and it is not possible for the international search to cover the entire subject-matter to which the claims are directed (Art. 6 and 17(2)(a)(ii) and Rule 33.3(b)).

3. Claims Nos.:

These claims lack conciseness and international search cannot reasonably be expected to cover the entire subject-matter to which the claims are directed (Art. 6 and Rule 33.3(b)).

4. Claims Nos.:

These claims are dependent claims which 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)