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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

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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: BIOLOGICALLY ACTIVE PEPTIDES

(57) Abstract: Thirty substantially pure and biologically active peptides are disclosed. Nucleic acids that have sequences coding for the biologically active peptides and pharmaceutical formulation produced therefrom are also disclosed.

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INTERNATIONAL SEARCH REPORT

Int nal Application No
PCT/GB 02/03203

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K7/06 C07K7/08 C07K5/107 C07K5/117 C07K5/087
C07K5/083 A61K38/04 C07K14/805 A61K38/42 C07K14/47
A61K38/17 A61P9/10 A61P37/02 A61P35/00 A61P31/20

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 C07K 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, EPO-Internal, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FOGACA E.A.: "Antimicrobial activity of bovine hemoglobin fragment in the tick Boophilus micrplus" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 36, 1999, pages 25330-25334, XP002236974 MD US The whole document; see especially Table III ---	1-4,6-27
X	KARELIN A A ET AL: "PROTEOLYTIC DEGRADATION OF HEMOGLOBIN IN ERYTHROCYTES LEADS TO BIOLOGICALLY ACTIVE PEPTIDES" PEPTIDES, ELMSFORD, US, vol. 16, no. 4, 1995, pages 693-697, XP000983865 ISSN: 0196-9781 see especially Table I --- -/--	1-4,6-27

[X] Further documents are listed in the continuation of box C.

[X] 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	Date of mailing of the international search report
20 June 2003	06 AUG 2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Groenendijk, M

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inte nal Application No
PCT/GB 02/03203

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61P3/04

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)

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 861 483 A (WOLPE STEPHEN D) 19 January 1999 (1999-01-19) See particularly claims 1-11; column 1, lines 5-17 ---	1-4,6-27
X	SCHALLY E.A.: "Isolation, structural elucidation and synthesis of a tetradecapeptide with in vitro ACTH-releasing activity corresponding to residues 33-46of the alpha-chain of porcine hemoglobin" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 82, no. 2, 1978, pages 582-588, XP008015843 ORLANDO, FL US the whole document --- -/--	1-4,6-27

[X] Further documents are listed in the continuation of box C.

[X] 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

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"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	Date of mailing of the international search report
20 June 2003	

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Groenendijk, M

INTERNATIONAL SEARCH REPORT

Int ›nal Application No
PCT/GB 02/03203

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	CHANG R C C ET AL: "ISOLATION AND STRUCTURE OF SEVERAL PEPTIDES FROM PROCINE HYPOTHALAMI" BIOCHIMICA ET BIOPHYSICA ACTA, AMSTERDAM, NL, vol. 625, 1980, pages 266-273, XP002905222 ISSN: 0006-3002 the whole document	1-4,6-9, 12-27
X	KARELIN A A ET AL: "'Proteolytic degradation of hemoglobin in erythrocytes results in formation of biologically active peptides!" BIOORGANICHESKAIA KHIMIIA. RUSSIA APR 1998, vol. 24, no. 4, April 1998 (1998-04), pages 271-281, XP008015845 ISSN: 0132-3423 See Table I and page 281, abstract	1-4,6-27
A	WO 98 12219 A (BERGSTRAND HAAKAN ;SAERNSTRAND BENGT (SE); ASTRA AB (SE); ERIKSSON) 26 March 1998 (1998-03-26) the whole document	1-27
A	WO 97 35602 A (SMITHKLINE BEECHAM PLC ;AL BARAZANJI KAMAL A (GB)) 2 October 1997 (1997-10-02) See especially page 1, paragraph 4	
X	LADRAM ET AL: "Characterization of receptors for thyrotropin-releasing hormone-receptors potentiating peptide on rat anterior pituitary membranes" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 267, no. 36, 25 December 1997 (1997-12-25), pages 25697-26702, XP002149258 ISSN: 0021-9258 See particularly Table II	1-17
X	SQUIRE E.A.: "Leucine aminopeptidase-like activity in Aplysia hemolymph rapidly degrades biologically active alpha-bag cell peptide fragments" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 266, no. 33, 25 November 1991 (1991-11-25), pages 22355-22363, XP002245007 MD US See especially tables 1 and 4	1-17

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INTERNATIONAL SEARCH REPORT

Inte ial Application No
PCT/GB 02/03203

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	FURKA A ET AL: "STRING SYNTHESIS A SPATIALLY ADDRESSABLE SPLIT PROCEDURE" JOURNAL OF COMBINATORIAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 2, no. 3, 19 May 2000 (2000-05-19), pages 220-223, XP001058980 ISSN: 1520-4766 table 3 ---	1-17
X	WO 00 63233 A (LINDERMAN RUSSELL J ;UNIV NORTH CAROLINA (US); BOROVSKY DOV (US);) 26 October 2000 (2000-10-26) See SEQ ID No 3 and claims 3,21,27,33 ---	1-17
A	BULANT M ET AL: "PROCESSING OF THYROTROPIN-RELEASING HORMONE PROHORMONE(PRO-TRH) GENERATES A BIOLOGICALLY ACTIVE PEPTIDE,PREPRO-TRH-(160-169), WHICH REGULATES TRH-INDUCED THYROTROPIN SECRETION" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 87, no. 12, 1 June 1990 (1990-06-01), pages 4439-4443, XP000134334 ISSN: 0027-8424 figure 1 -----	1-17

INTERNATIONAL SEARCH REPORT

national application No.
PCT/GB 02/03203

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 26 and 27 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. [X] Claims Nos.: 1-4,6-27(partially)
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:

see additional sheet

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. [X] 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.:

1-27(all partially)

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.

[X] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/GB 02 03203

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-4,6-27(partially)

The initial phase of the search for subject 11 revealed a very large number of compounds(over 180000) and related documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to the SEQ ID NOs 14 and 16 and their use.

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. Claims: 1-30(all partially)

   Peptides comprising the sequence SEQ ID No.1, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

2. Claims: 1-30(all partially)

   Peptides comprising the sequence SEQ ID No.2, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

3. Claims: 1-30(all partially)

   Peptides comprising the sequence SEQ ID No.3, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

4. Claims: 1-30(all partially)

   Peptides comprising one of the sequences SEQ ID No.4,6,29 or 30, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

5. Claims: 1-30(all partially)

   Peptides comprising the sequence SEQ ID No.5, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

6. Claims: 1-30(all partially)

   Peptides comprising the sequence SEQ ID No.7, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

7. Claims: 1-30(all partially)

   Peptides comprising the sequence SEQ ID No.8, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

8. Claims: 1-30(all partially)

   Peptides comprising the sequence SEQ ID No.9, their

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

9. Claims: 1-30(all partially)

Peptides comprising one of the sequences SEQ ID No.10-12, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

10. Claims: 1-30(all partially)

Peptides comprising the sequence SEQ ID No.13, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

11. Claims: 1-30(all partially)

Peptides comprising one of the sequences SEQ ID No.14 or 16, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

12. Claims: 1-30(all partially)

Peptides comprising the sequence SEQ ID No.15, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

13. Claims: 1-30(all partially)

Peptides comprising the sequence SEQ ID No.17, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

14. Claims: 1-30(all partially)

Peptides comprising one of the sequences SEQ ID No.18-23, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

15. Claims: 1-30(all partially)

Peptides comprising the sequence SEQ ID No.24, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

16. Claims: 1-30(all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Peptides comprising the sequence SEQ ID No.25, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

17. Claims: 1-30(all partially)

Peptides comprising the sequence SEQ ID No.26, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

18. Claims: 1-30(all partially)

Peptides comprising the sequence SEQ ID No.27, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

19. Claims: 1-30(all partially)

Peptides comprising the sequence SEQ ID No.28, their derivatives, DNA encoding said compounds, their pharmaceutical compositions, preparations and use.

INTERNATIONAL SEARCH REPORT

formation on patent family members

Int ıal Application No
PCT/GB 02/03203

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		AU 2439197 A	22-10-1997
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		CN 1220670 A	23-06-1999
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		WO 0063233 A2	26-10-2000