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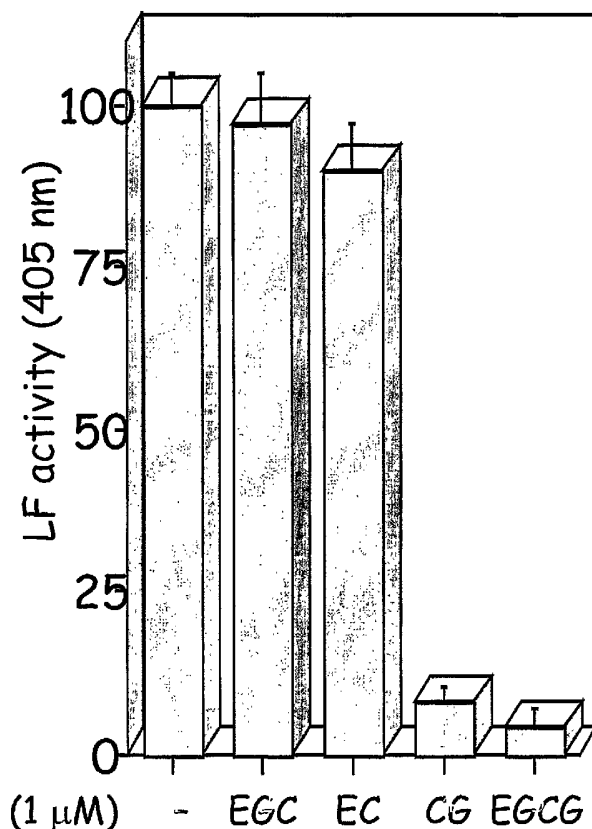
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- (71) Applicant and
(72) Inventor: **MONTECUCCO, Cesare** [IT/IT]; Dipartimento de Scienze Biomediche, Università di Padova, Via G. Colombo 3, I-35121 Padova (IT).
- (74) Agents: **MARSHALL, J., Cameron et al.**; Carpmaels & Ransford, 43-45 Bloomsbury Square, London WC1A 2RA (GB).
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[Continued on next page]

(54) Title: GREEN TEA AND OLYPHENOL INHIBITORS OF BACTERIAL PROTEASES



(57) Abstract: The use of green tea extract and/or polyphenols as protease inhibitors, in particular as metalloprotease inhibitors, in the treatment of bacterial infections associated with protease activity, in particular for the treatment or prevention of anthrax. Preferred polyphenols are those extractable from green tea, in particular catechins and especially catechin gallate and (-)-epigallocatechin gallate.



FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB2004/001997

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K35/78 A61P31/04

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)

IPC 7 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)

EPO-Internal, WPI Data, PAJ, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	DELL'AICA ISABELLA ET AL: "Potent inhibitors of anthrax lethal factor from green tea." EMBO REPORTS. APR 2004, vol. 5, no. 4, April 2004 (2004-04), pages 418-422, XP002297697 ISSN: 1469-221X the whole document	1-6,10, 11
X	DE 196 27 344 A (VITASYN GMBH ENTWICKLUNG & VER) 8 January 1998 (1998-01-08) page 2, line 28 - line 55	1-4,10, 11
Y	page 3, line 40 - line 44	5,6
X	EP 0 397 914 A (MITSUI NORIN KK) 22 November 1990 (1990-11-22)	1-4,10, 11
Y	claims; examples	5,6
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☒ 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
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- *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.
- *G* document member of the same patent family

Date of the actual completion of the international search

23 September 2004

Date of mailing of the international search report

26. 01. 2005

Name and mailing address of the ISA

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

Authorized officer

Winger, R

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB2004/001997

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 0181, no. 70 (C-1182), 23 March 1994 (1994-03-23) & JP 5 336939 A (ASAHI BREWERIES LTD), 21 December 1993 (1993-12-21) abstract -----	1-4,10, 11
X	TAYLOR PETER W ET AL: "New ways to treat bacterial infections." DRUG DISCOVERY TODAY, vol. 7, no. 21, 1 November 2002 (2002-11-01), pages 1086-1091, XP002297698 ISSN: 1359-6446 page 1088, column 2 -----	1-4,10, 11
Y	ASCENZI P ET AL: "Anthrax toxin: A tripartite lethal combination" FEBS LETTERS 20 NOV 2002 NETHERLANDS, vol. 531, no. 3, 20 November 2002 (2002-11-20), pages 384-388, XP004392673 ISSN: 0014-5793 page 385, column 2, paragraph 2 page 387, column 1, paragraph 3 - column 2, paragraph 1 -----	5,6,10, 11
Y	BENELLI ROBERTO ET AL: "Anti-invasive effects of green tea polyphenol epigallocatechin-3-gallate (EGCG), a natural inhibitor of metallo and serine proteases" BIOLOGICAL CHEMISTRY, vol. 383, no. 1, January 2002 (2002-01), pages 101-105, XP009037060 ISSN: 1431-6730 page 104, last paragraph; figure 1 -----	5,6,10, 11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2004/001997

Box 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:

Although claims 1, 3, 5, 6, 10 and 11 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 composition.
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 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 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.:

1-6, 10, 11

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

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

1. claims: 1-6,10,11

Method for the treatment of bacterial infection and method for inhibiting the proteolytic cleavage of a mitogen activated protein kinase kinase, respectively, comprising administering green tea extracts or polyphenols.

2. claims: 7-9

Composition comprising a bacterial protease and a polyphenol.

3. claim: 12

Compounds of formula I, II or III.

4. claims: 13,14

Crystal of a protease and a polyphenol.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/

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Continuation of Box 3.

Although claims 1, 3, 5, 6, 10 and 11 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 composition.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International Application No
PCT/IB2004/001997

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
DE 19627344	A	08-01-1998	DE	19627344 A1	08-01-1998
			DE	29623606 U1	10-06-1999
EP 0397914	A	22-11-1990	JP	2304079 A	17-12-1990
			JP	2846657 B2	13-01-1999
			JP	2306915 A	20-12-1990
			JP	2986805 B2	06-12-1999
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