

(43) International Publication Date
24 August 2006 (24.08.2006)

PCT

(10) International Publication Number
WO 2006/088385 A3(51) International Patent Classification:
A61K 36/00 (2006.01)(21) International Application Number:
PCT/RO2006/000003(22) International Filing Date:
15 February 2006 (15.02.2006)

(25) Filing Language: English

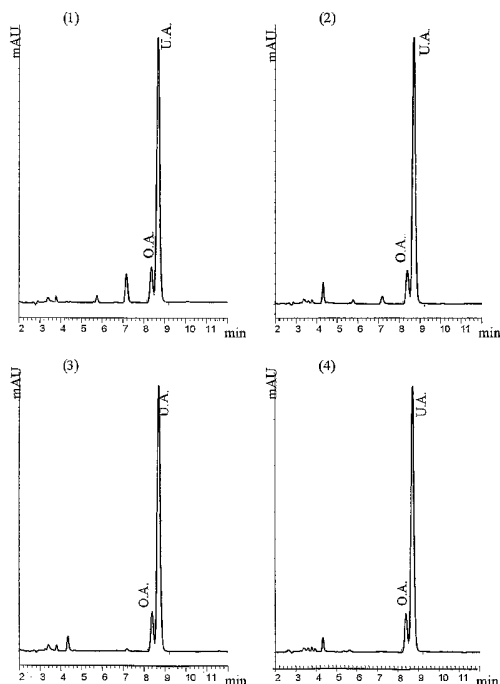
(26) Publication Language: English

(30) Priority Data:
a 2005 00117 18 February 2005 (18.02.2005) RO(71) Applicant (for all designated States except US): S.C.
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140, R-061567 Bucharest 6 (RO).(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
UZ, VC, VN, YU, ZA, ZM, ZW.(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,

[Continued on next page])

(54) Title: BIOACTIVE COMPLEX OF TRITERPENE ACIDS, ITS PRODUCTION PROCESS AND MEDICINAL PRODUCTS
WITH THERAPEUTICAL USES

Chromatograms for bioactive complex of triterpene acids produced from:
(1) Salvia Sp., (2) Lavandula Sp., (3) Sambucus Nigra, (4) Crataegus Sp.;
O.A. = oleanolic acid; U.A. = ursolic acid.

(57) Abstract: The invention relates to a bioactive complex of triterpene acids, as such or in the form of Na, K, NH₄ salts of minimum 90 % purity, with a standardized content formed of: minimum 75 % ursolic acid, 10...15 oleanolic acid and 4...10 % other triterpene acids consisting of one or more of the following acids: hydroxyursolic, hydroxyoleanolic, betulinic, dehydrobetulinic, produced from the plants *Salvia sp.*, *Lavandula sp.*, *Sambucus nigra* and *Crataegus sp.* The production process recommends increase of selectivity and efficiencies of extraction, purification and crystallization steps by using structured waters ("I" - acid pH water and "S" - alkaline pH water) in the composition of solvents used. The bioactive complex of triterpene acids has a marked and diversified pharmacological activity for bioregulating proteinic, glucidic and lipidic metabolism, particularly on aged organisms, as well as immunoprotective, antioxidizing, hepatoprotective, and retarding activity in tumour progression, being conditioned as new medicinal products for internal and/or external use with applicability in human and veterinary therapy.



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, 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).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report*

(88) Date of publication of the international search report:

28 December 2006

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/R02006/000003

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K36/00

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)
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, MEDLINE, EMBASE, PASCAL, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 200414 Derwent Publications Ltd., London, GB; Class B04, AN 2004-133431 XP002389427 & CN 1 439 648 A (MEDICINAL PLANT INST CHINESE ACAD MEDICA) 3 September 2003 (2003-09-03) abstract	1,3,6-12
X	DATABASE WPI Section Ch, Week 198213 Derwent Publications Ltd., London, GB; Class B04, AN 1982-25087E XP002389428 & JP 57 031620 A (JUNISHO N) 20 February 1982 (1982-02-20) abstract	1,3,6-12

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☒ 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 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

1 August 2006

Date of mailing of the international search report

11/08/2006

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INTERNATIONAL SEARCH REPORT

International application No

PCT/R02006/000003

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TANIGUCHI S ET AL: "Production of bioactive triterpenes by Eriobotrya japonica calli" February 2002 (2002-02), PHYTOCHEMISTRY, PERGAMON PRESS, GB, PAGE(S) 315-323 , XP004335024 ISSN: 0031-9422 the whole document -----	1,3,6-12
X	JU J-H ET AL: "Studies on constituents of triterpene acids from Eriobotrya japonica and their anti-inflammatory and antitussive effects" 2003, CHINESE PHARMACEUTICAL JOURNAL 2003 CHINA, VOL. 38, NR. 10, PAGE(S) 752-757 , XP009068958 ISSN: 1001-2494 the whole document -----	1,3,6-12
X	URECH K ET AL: "Apoptosis inducing activity of viscin, a lipophilic extract from Viscum album L." January 2005 (2005-01), JOURNAL OF PHARMACY AND PHARMACOLOGY, VOL. 57, NR. 1, PAGE(S) 101-109 , XP009068957 ISSN: 0022-3573 the whole document -----	1,3,6-12
X	SETZER WILLIAM N ET AL: "Biologically active triterpenoids of Syncarpia glomulifera bark extract from Paluma, north Queensland, Australia" March 2000 (2000-03), PLANTA MEDICA, VOL. 66, NR. 2, PAGE(S) 176-177 , XP009068960 ISSN: 0032-0943 the whole document -----	1,3,6-12
X	SOUSA MENEZES DE F ET AL: "CHEMICAL CONSTITUENTS FROM MARSYPIANTHES CHAMAEDRYS" ANAIIS DA ACADEMIA BRASILEIRA DE CINCIAS, ACADEMIA BRASILEIRA DE CINCIAS, RIO DE JANEIRO, BR, vol. 70, no. 4, 1998, pages 761-766, XP000929286 ISSN: 0001-3765 the whole document -----	1,3,6-12
X	COSTA V B ET AL: "Anti-inflammatory and analgesic activity of Bouchea fluminensis." June 2003 (2003-06), FITOTERAPIA, VOL. 74, NR. 4, PAGE(S) 364-371 , XP009069234 ISSN: 0367-326X the whole document -----	1,3,6-12

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INTERNATIONAL SEARCH REPORT

International application No
PCT/R02006/000003

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIU J ET AL: "THE EFFECTS OF 10 TRITERPENOID COMPOUNDS ON EXPERIMENTAL LIVER INJURY IN MICE" FUNDAMENTAL AND APPLIED TOXICOLOGY, SOCIETY OF TOXICOLOGY, AKRON, OH, US, vol. 22, no. 1, 1994, pages 34-40, XP009069262 ISSN: 0272-0590 the whole document -----	1,3,6-12

INTERNATIONAL SEARCH REPORT

International application No.
PCT/R02006/000003

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:
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:
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 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:

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 II.2

Applicant's attention is drawn to the fact that claims 1-5 are drafted in the form of a "product-by-process" claim. Hence the product per se must be novel and inventive etc. independently from the process by which it is obtained. Thus, the origin from the plant species as claimed (i.e. Salvia etc.) is not limiting.

Furthermore, Applicant's attention is drawn to the fact that the term "such as" used in claim 1 ("4...10% other triterpene acids such as...") is not limiting contrary to the phrasing "consisting of" used e.g. in claim 2. Hence, a violation of Article 5 and/or 6 PCT is objected.

In addition, it is pointed out to the Applicant that the wording of claims 1-12 is unclear with respect to the amounts, since it reads "a minimum 90% content of triterpene acids represented by...". The following listing, however, comprises a minimum of 75% ursolic acid, 10 % oleanolic acid and 4 % other triterpene acids, this sums up to 89 %

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/R02006/000003

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
CN 1439648	A	03-09-2003	NONE	
JP 57031620	A	20-02-1982	JP 1437049 C	25-04-1988
			JP 62042582 B	09-09-1987