



- (51) International Patent Classification:
C07C 49/733 (2006.01) C07C 49/743 (2006.01)
- (21) International Application Number:
PCT/US2012/040379
- (22) International Filing Date:
1 June 2012 (01.06.2012)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
61/493,250 3 June 2011 (03.06.2011) US
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- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,

[Continued on next page]

(54) Title: HYPERFORIN ANALOGS, METHODS OF SYNTHESIS, AND USES THEREOF

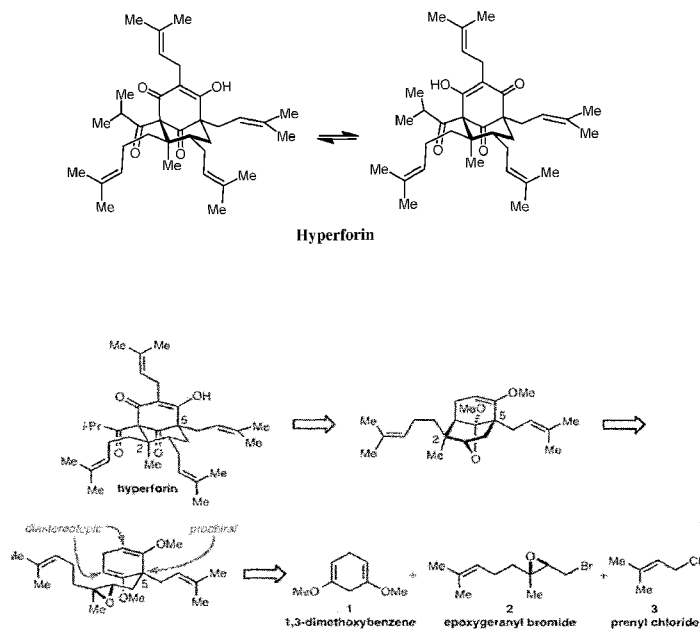


Figure 1

(57) Abstract: The present invention provides a novel 11-step enantioselective approach to the natural product hyperforin, which enables access to a wide variety of hyperforin analogs. The present invention also provides pharmaceutical compositions comprising inventive hyperforin analogs. Hyperforin analogs synthesized using the present synthetic method are envisioned useful in the treatment of various conditions, including, but not limited to, depression and conditions characterized by depression, inflammatory skin conditions, diabetes, asthma, chronic obstructive pulmonary disease (COPD), kidney disorders, and ischemic brain damage.



EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))*

Published:

— *with international search report (Art. 21(3))*

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

25 April 2013

A. CLASSIFICATION OF SUBJECT MATTER*C07C 49/733(2006.01)i, C07C 49/743(2006.01)i*

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)

C07C 49/733; C07C 49/693; A61K 31/00; A61K 35/00; C07C 49/105; C07C 49/403; A61K 35/78; C07C 49/653; A61K 31/22; C07C 49/477

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & Keywords:hyperforin, depression, inflammatory skin conditions, diabetes, asthma, chronic obstructive pulmonary disease, kidney disorders and ischemic brain damage

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00-54785 A2 (SHAMAN PHARMACEUTICALS, INC.) 21 September 2000 See abstract, compounds 1a-3a, page 35, line 16-page 42, line 22 and claims 4-46.	1-14, 47, 48
X	WO 00-54760 A2 (SHAMAN PHARMACEUTICALS, INC.) 21 September 2000 See abstract and claims 1-22.	1-14, 47, 48
X	US 2005-0165117 A1 (EZIO BOMBARDELLI et al.) 28 July 2005 See abstract, compounds Ib-II, paragraph [0027], examples 2-6 and claims 1-9.	1-14, 47, 48
X	WO 99-64388 A1 (INDENA S.P.A.) 16 December 1999 See abstract, claims 1-6, examples 2 and 3.	1-14, 47, 48
X	WO 03-091193 A1 (INDENA S.P.A. et al.) 06 November 2003 See abstract and claims 1-7.	1-14, 47, 48
X	US 2005-0090693 A1 (SIEGFRIED SEEGER et al.) 28 April 2005 See abstract, paragraph [0046], formulae Ia-Id and claim 2.	1-3, 11

 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 application or patent 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 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

26 FEBRUARY 2013 (26.02.2013)

Date of mailing of the international search report

27 FEBRUARY 2013 (27.02.2013)

Name and mailing address of the ISA/KR

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Box No. 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.: 18, 19 and 21-25
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 18, 19 and 21-25 pertain to method for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.
2. Claims Nos.: 16, 17 and 22
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:
Claims 16, 17 and 22 are unclear under PCT Article 6, because they refer to any one of multiple dependent claims which are not drafted in accordance with the third sentence of PCT Rule 6.4(a).
3. Claims Nos.: 15, 18-21 and 23-25
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. 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 the extra 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.:
1-17, 20, 47 and 48

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2012/040379

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 00-54785 A2	21.09.2000	AU 2000-37387 A1	04.10.2000
		WO 00-54785 A3	03.05.2001
WO 00-54760 A2	21.09.2000	AU 2000-37441 A1	04.10.2000
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		JP 2005-515979 A	02.06.2005
		US 7199161 B2	03.04.2007
		WO 03-043622 A1	30.05.2003

This International Searching Authority found multiple inventions in this application, as follows:

Invention Group I (Claims 1-17, 20, 47 & 48): A compound of Formula (I) or (II) (or (K-1) or (Q-1)), a pharmaceutical composition comprising the same, or a method of treating depression (or a condition) comprising the same.

Invention Group II (Claims 26-42): A compound of Formula (F-1) and a method of preparing the same.

Invention Group III (Claims 43-44): A compound of Formula (E-1) or (E-2).

Invention Group IV (Claims 45-46): A compound of Formula (G-1) or (J-1).

There is no common technical feature linking invention groups I and III together. The common technical feature linking inventions groups I, II and IV is bicyclo[3,3,1]nonane structure, which is already disclosed in prior art documents such as US 2005-0090693 A1 (28 April 2005), WO 2000-054760 A2 (21 September 2000) and WO 2000-054785 A2 (21 September 2000). Thus, the invention groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because no common technical feature contributes over the prior art within the meaning of PCT Rule 13.2.