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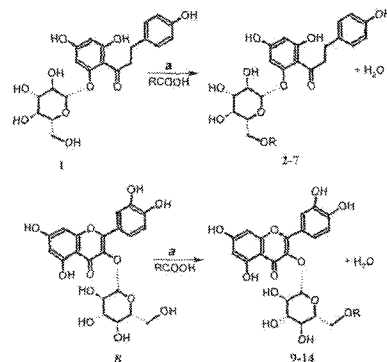
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(88) Date of publication of the international search report:

25 June 2015

(54) Title: ACYLATED DERIVATIVES OF PHLORIDZIN AND ISOQUERCETRIN AS ANTICANCER THERAPEUTICS AND METHODS OF USE THEREOF

FIG. 1



a) Acetone, 3 Å molecular sieves, Novozyme 435[®], 45 °C, stirring, 24 h; R = Oleic, Stearic, Linoleic, Linolenic, Eicosapentaenoic (EPA), and Docosahexaenoic acids or their esters

Scheme 1

(57) Abstract: The present specification is directed to an acylated flavonoid derivative derived from natural or synthetic flavonoids such as phloridzin and isoquercitrin, and long chain fatty acids, mon- or poly- unsaturated once in particular. The acylated flavonoid derivatives can be part of a pharmaceutical composition. Method of decreasing proliferation and viability of cancer cells in a subject include administering the disclosed pharmaceutical composition.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2014/002520

A. CLASSIFICATION OF SUBJECT MATTER

IPC: **C07H 15/203** (2006.01), **A61K 31/7034** (2006.01), **A61K 31/7048** (2006.01), **A61P 35/00** (2006.01),
A61P 35/02 (2006.01)

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: **C07H 15/203** (2006.01), **A61K 31/7034** (2006.01), **A61K 31/7048** (2006.01), **A61P 35/00** (2006.01),
A61P 35/02 (2006.01)

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

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

CAplus, Questel-Orbit, Canadian Patent Database, Scopus

Flavonoid, glucoside, glucoside, fatty acid, ester, isoquercitrin, phloridzin, estification, acylation, anticancer, anti-proliferative

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SALEM et al, "Effect of acyl donor chain length on isoquercitrin acylation and biological activities of corresponding esters", <i>Process Biochemistry</i> , 45 (3), 2010, 382-389. Fig. 1, p. 385; Fig. 6, p. 387.	1-20
X	ZIAULLAH et al, "Biocatalytic synthesis, structural elucidation, antioxidant capacity and tyrosinase inhibition activity of long chain fatty acid acylated derivatives of phloridzin and isoquercitrin", <i>Bioorg Med Chem</i> , 21(3), 1 February 2013, 684-692. cmpd. 2-7, 9-14, scheme 2, p. 690.	1-3
X	ZIAULLAH, et al, "An efficient microwave-assisted enzyme-catalyzed regioselective synthesis of long chain acylated derivatives of flavonoid glycosides", <i>Tetrahedron Lett</i> , 54(15), 10 April 2013, 1933-1937. cmpd. 2-7, 9-14, table 2, p. 1935.	1-3

☒ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* "A" "E" "L" "O" "P"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance earlier application or patent but published on or after the international filing date 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) document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed	"T" "X" "Y" "&"	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 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 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
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Date of the actual completion of the international search
02 March 2015 (02-03-2015)

Date of mailing of the international search report
12 March 2015 (12-03-2015)

Name and mailing address of the ISA/CA
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2014/002520

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P	NAIR et al, "Fatty acid esters of phloridzin induce apoptosis of human liver cancer cells through altered gene expression", PLoS ONE, 9(9), 17 September 2014, Article number e107149.	1-20

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2014/002520**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the 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. ☒ Claim Nos.: 9-19
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 9-19 are directed to a method for treatment of the human or animal body by surgery or therapy, which the International Searching Authority is not required to search under Rule 39.1(iv) of the PCT. However, this Authority has carried out a search based on the alleged effect or purpose/use of the product defined in claims 9, 15, 17.
2. ☐ Claim 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. ☐ Claim Nos.:
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:

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 additional fees, this Authority did not invite payment of additional fees.
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 claim 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 claim Nos.:

- 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.