

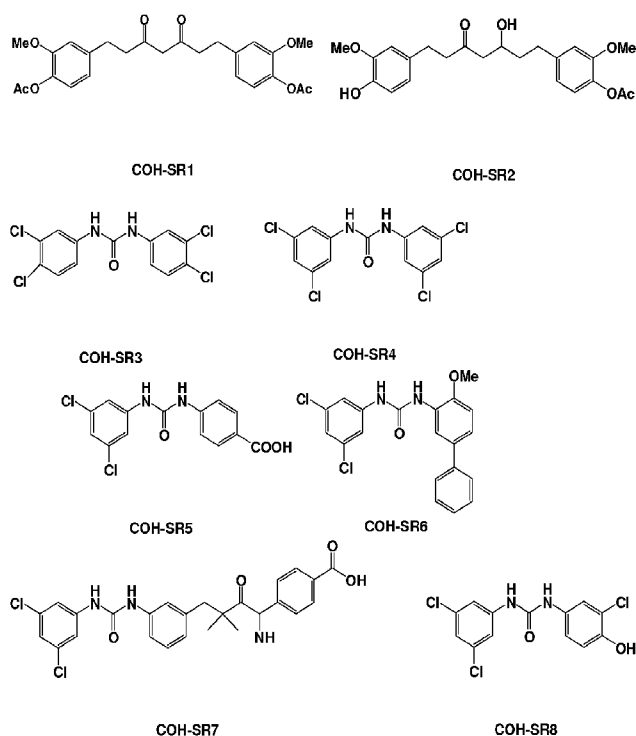


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MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
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[Continued on next page]

(54) **Title:** NOVEL MODULATORS OF DEVELOPMENT OF ADIPOCYTE AND CANCER CELLS

Figure 1



(57) **Abstract:** One aspect of the disclosure relates to derivatives of aryl and heterocyclicureido aryl and heterocyclic carboxamido isobutyric acids, dichlorophenyl urea, curcumin, and 1,3-diazetidine-2,4-dione, and pharmaceutical compositions thereof. The derivatives disclosed herein can modulate development of adipocytes and various cancer cells, including resistant cancer cells and cancer stem cells. Another aspect of the disclosure relates to the use of the derivatives and pharmaceutical compositions disclosed herein in treatment of obesity and various cancers.

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20 September 2012

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

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/23034

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A01N 47/28; A61K 31/17 (2012.01)

USPC - 514/596

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)
USPC: 514/596Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 514/457, 559, 563, 584, 588, 613 (see search terms below)

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

PubWEST (PGPB,USPT,EPAB,JPAB,DWPI): sr1|cosr1]?co-sr1? leukemia|tumor|antitumor|antileukemia|cancer|anticancer; rtk|kinase; modulate|impair|inhibit obesity; urea, dichloro, COH-SR4, dichlorophenyl, bisphenylurea, diphenylurea, bisphenyl, diphenyl, AC1LC6PF, AC1Q3IF6, ZINC10277685, AKOS003538010, EN30-35574, T6330004

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PUBCHEM Compound ID 10994120 (PubChem 10994120 Create date 2006-10-26 (online) [retrieved on 2012-07-02]. Retrieved from internet: <URL: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?q=all&cid=10994120#ec>	1
Y	US 5,773,459 A (Cho et al.) 30 June 1998 (30.06.1998) col 2, ln 35-44; col 3, ln 2, ln 49; col 4-10; col 10, ln 30-35; col 12, ln 44-50; col. 6, ln 35-48	2-9, 11, 14-15
Y	US 2009/0202529 A1 (Threadgill et al.) title	2-9, 11, 14-15
Y	US 2009/0202529 A1 (Threadgill et al.) title	5-6
A	US 4,233,450 A (Sholz) 11 November 1980 (11.11.1980) col 2, ln 40	1-8, 11, 14-15
A	RAHBAR et al. Novel Inhibitors Of Advanced Glycation Endproducts. Archives of Biochemistry and Biophysics, 2003, Vol 419, pp 63-79; pg 63-64	2-9, 11, 14-15
A	STORZ. Reactive Oxygen Species In Tumor Progression. Frontiers in Bioscience, 2005, Vol 10, pp 1881-1896; pg 1889	2-9, 11, 14-15
A	FURUKAWA et al. Increased Oxidative Stress In Obesity And Its Impact On Metabolic Syndrome. Journal of Clinical Investigation, 2004, Vol 114(12), pp 1752-1761; pg 1756	2, 5-6

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

* 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 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

02 July 2012 (02.07.2012)

Date of mailing of the international search report

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Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/23034

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.:
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:

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 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 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 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 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.:
1-9, 11 and 14-15

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

International application No.

PCT/US 12/23034

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I+: claims 1-20, COH-SR compound selected from the group consisting of COH-SR1, COHSR2, COH-SR3, COH-SR4, COH-SR5, COH-SR6, COH-SR7, COH-SR8, COH-SR9, COH-SR10, COH-SR11, COH-SR12, COH-SR13, COH-SR14, COH-SR16, COH-SR18, LR23, LR59, and the pharmaceutically acceptable derivative, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios, etc., limited to one the first of the COH-SR compounds listed (COH-SR1).

The inventions listed as Group I+ do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The claims of the various groups as defined above do not share any special technical feature that is an advance over the prior art. US 4,233,450 A (Sholz) discloses COH-SR4 (bis-(3,5-dichlorophenyl)-urea - see instant fig. 2 or para [0077]). See Sholz col 2, ln 40. Furthermore, the article entitled "Novel Inhibitors Of Advanced Glycation Endproducts" by Rahbar et al. (hereinafter 'Rahbar') discloses the compounds LR23 and LR59 (pg 70-71).

Thus, the inventions listed as Groups I+ do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding special technical feature. According to PCT Rule 13.2, unity of invention exists only when the same or corresponding technical feature is shared by all claimed inventions.

In this case the first named invention and first named species that will be searched without additional fees is Group I represented by claims 1-20, limited to the first COH-SR compound listed in claim 1, namely claims 1-9, 11 and 14-15.

In order for more than one species (invention) to be examined, the appropriate additional examination fees must be paid and the desired species clearly identified.

Therefore, the inventions of Groups I+ lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.