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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: NOVEL PPAR LIGANDS THAT DO NOT CAUSE FLUID RETENTION, EDEMA OR CONGESTIVE HEART FAIL-
URE

(57) Abstract: Methods are provided for treating or prophylactically preventing metabolic disorders in humans without causing, promoting, or aggravating fluid retention, peripheral edema, pulmonary edema, or congestive heart failure, by administration of a therapeutically effective amount of a compound sufficient to partially or fully activate peroxisome proliferator activated receptors (PPARs) and partially or fully inhibit, antagonize or block the activity of angiotensin II type 1 receptors. Metabolic disorders that can be treated or prevented include but are not limited to type 2 diabetes, the metabolic syndrome, prediabetes, and other insulin resistance syndromes. Compounds are provided that antagonize or block the angiotensin II type 1 (AT1) receptor, function as partial or full activators of peroxisome proliferator activated receptors (PPARs), can be used to treat or prevent diseases known to be treatable or preventable by PPAR activators and were not previously recognized to be therapeutic targets for angiotensin II receptor antagonists.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/24881

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/41, 31/415, 49/00

US CL : 424/9.2; 514/381, 387

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)
U.S. : 424/9.2; 514/381, 387

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 practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database HCAPLUS on STN (Columbus, OH, USA), 133:41183, VAMECQ, J et al, 'Peroxisome proliferator-activated receptors (PPARs) and their implications in diseases,' Current Opinion in Endocrinology & Diabetes, 2000, 7(1), 8-18, abstract.	1-18
Y	Database MEDLINE on STN, (Columbus, OH, USA), 22006210, DIEP, Q. et al, 'Structure, endothelial function, cell growth, and inflammation in blood vessels of angiotensin II-infused rats: role of peroxisome proliferator-activated receptor-gamma,' Circulation, 14 May 2002, 105(19), 2296-302, abstract, especially Conclusions.	1-6

☐ 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	"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
"B" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"Z" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No.

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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
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 II Observations where unity of invention is lacking (Continuation of Item 2 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.

INTERNATIONAL SEARCH REPORT

PCT/US03/24881

Continuation of B. FIELDS SEARCHED Item 3:
REGISTRY, HCAPLUS, MEDLINE, EMBASE
search terms: peroxisome proliferator, ppar, angiotensin receptors