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Published
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31 August 2000 (31.08.00)

(54) Title: PYRAZOLES AS ESTROGEN RECEPTOR MODULATORS

(57) Abstract

Estrogen receptor–modulating pyrazole compounds are described in addition to methods and compositions for treating or preventing estrogen receptor–mediated disorders. The compounds described have been found to have unexpected and surprising activity in modulating estrogen receptor activity. Thus, the compounds of the present invention have utility in preventing or treating estrogen receptor–mediated disorders such as osteoporosis, breast and endometrial cancers, atherosclerosis, and Alzheimer's disease.

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INTERNATIONAL SEARCH REPORT

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PCT/US 99/17799

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D231/12 C07D401/04 C07D403/04 C07D471/04 C07D413/04
C07D409/04 C07D231/56 C07D231/54 C07D231/18 A61K31/415
//(C07D471/04,231:00,213:00)

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)
IPC 7 C07D A61K

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WAECHTER, GERALD A. ET AL: "Tetrahydronaphthalenes: Influence of Heterocyclic Substituents on Inhibition of Steroidogenic Enzymes P450 arom and P450 17" J. MED. CHEM. (1996), 39(4), 834-41 , XP002099563 table 1 ---	54-69
X	DE 42 30 839 A (CIBA GEIGY AG) 25 March 1993 (1993-03-25) page 7, line 2 - line 22; examples ---	3,5-7
X	DE 41 26 543 A (CHEM & PHARM PATENT HOLD LTD) 11 February 1993 (1993-02-11) claim 1; examples ---	3,5-7
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 May 2000	23/05/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	De Jong, B

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INTERNATIONAL SEARCH REPORT

Int. tional Application No
PCT/US 99/17799

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 442 448 A (SQUIBB BRISTOL MYERS CO) 21 August 1991 (1991-08-21) page 23 ---	3,5-7
X	DE 24 41 504 A (AMERICAN CYANAMID CO) 20 March 1975 (1975-03-20) page 14; claim 1 ---	3,5-7
X	FR 2 104 932 A (FERLUX) 28 April 1972 (1972-04-28) claims; examples ---	3,5-7
X	DATABASE CHEMABS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US BASS, R. G. ET AL: "Synthesis of poly(arylene ether pyrazoles) by aromatic nucleophilic displacement reactions" retrieved from STN Database accession no. 115:184050 XP002136354 see compound with RN=136788-48-2 & POLYM. PREPR. (AM. CHEM. SOC., DIV. POLYM. CHEM.) (1991), 32(2), 160-1 , ---	3
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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/US 99/17799

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	FINK, BRIAN E. ET AL: "Novel structural templates for estrogen -receptor ligands and prospects for combinatorial synthesis of estrogens" CHEM. BIOL. (1999), 6(4), 205-219 , 18 March 1999 (1999-03-18), XP000905542 the whole document	2-9, 56-69

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INTERNATIONAL SEARCH REPORT

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 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. [X] Claims Nos.: 56-69
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 56-69 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds.

2. [X] 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 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1,10-14,22,23,30,37-40,47

Present claims 1,10-14,22,23,30,37-40,47 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds according to claims 2-9,15-21,24-29,31-36,41-46,48-53.

The initial phase of the search for these claims revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of claims 2-9,15-21,24-29,31-36,41-46,48-53 (compounds per se) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). Consequently the search report with regard to said claims 2-9,15-21,24-29,31-36,41-46,48-53 has been limited to a selection of retrieved novelty -affecting documents,with a special emphasis to compounds containing at least one hydroxyphenyl substituent as illustrated by the examples of the application.

It should however be noted that the search and the search report can be considered as covering all claimed compounds of the prior art insofar these compounds display an estrogen receptor modulating activity.

The applicant's attention is drawn to the fact that claims, or parts of 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. ..tional Application No
PCT/US 99/17799

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