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CA, CH, 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,
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- with international search report (Art. 21(3))
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(88) Date of publication of the international search report:

29 October 2009

(54) Title: PREPARATION OF 6-OXA-8ALPHA-STEROID ESTROGEN ANALOGUES - A NEW GROUP OF UNNATURAL ESTROGENS AND THEIR USE IN MEDICINE

(57) Abstract: The invention is related to the area of new 6-Oxa-8 α -steroid estrogen analogues and the synthesis of these new biological active steroid estrogen analogues, namely, to the preparation of 6-oxa-8 α -steroid estrogens and their use as estrogen receptor modulators. These new estrogen analogues are ligands for estrogen receptors and as such may be useful for the treatment and prevention of a variety of conditions related to estrogen functioning. These conditions include bone and cartilage disorders, increased levels of LDL cholesterol, cardiovascular diseases, impairment of cognitive function, cerebral degeneration disorders, endometriosis and other types of inflammation, the metabolic syndrome, and cancer, in particular of the breast, uterus and prostate.



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INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. C07J73/00 A61K31/566 A61K31/56 A61P5/30

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)

C07J A61K A61P

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)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	A. G. SHAVVA, K. V. VLASOVA, S. B. TSOGOEVA, M. S. EGOROV AND P. P. YAKUTSENI: "A Study of the Binding of Estradiol and 8-Isoestradiol to the Estrogen ?-Receptor by Molecular Modeling" RUSSIAN JOURNAL OF BIOORGANIC CHEMISTRY, vol. 28, no. 3, May 2002 (2002-05), pages 209-214, XP002522563 cited in the application page 210; compounds XXV-XXVIII	1,2,4,9, 13,15, 20,23-26
X	GB 1 069 845 A (SMITH HERCHEL) 24 May 1967 (1967-05-24) cited in the application page 3; example 1	1-3,13, 14,23-26
Y		1,2,4, 13,15, 23-26
	----- -/-	

☒ 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 document 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

10 August 2009

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31/08/2009

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/009619

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 479 344 A (HUGHES GORDON ALAN ET AL) 18 November 1969 (1969-11-18) column 12; example 19 figure 1; compounds VI-VII -----	1-3, 13, 14, 23-26
X	SMITH, H. ET AL: "Total synthesis of derivatives of (+/-)-6-oxa and aza-estrone" EXPERIENTIA, vol. 20, no. 8, 1964, pages 418-419, XP008104977 page 419; compound XI -----	1, 3, 13, 14, 23-26
Y	A.G. SHAVVA ET AL.: "Synthesis and biological properties of D-homo-6-oxa-8?-analogues of steroid estrogens" RUSSIAN JOURNAL OF BIOORGANIC CHEMISTRY, vol. 33, no. 3, 4 June 2007 (2007-06-04), pages 288-292, XP002540389 page 289; compound IIIA -----	1, 2, 9, 13, 20, 23-26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2008/009619

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 additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an 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.:

1-2(part), 3-4, 9, 13(part), 14-15, 20, 23-26(part)

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 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-2 (part), 3, 13 (part), 14, 23-26 (part)

compound of formula II, its use as a medicament and process for preparing it

2. claims: 1-2 (part), 4, 13 (part), 15, 23-26 (part)

compound of formula IV, its use as a medicament and process for preparing it

3. claims: 1-2 (part), 5, 13 (part), 16, 23-26 (part)

compound of formula VI, its use as a medicament and process for preparing it

4. claims: 1-2 (part), 6, 13 (part), 17, 23-26 (part)

compound of formula VIII, its use as a medicament and process for preparing it

5. claims: 1-2 (part), 7, 13 (part), 18, 23-26 (part)

compound of formula X, its use as a medicament and process for preparing it

6. claims: 1-2 (part), 8, 13 (part), 19, 23-26 (part)

compound of formula XII, its use as a medicament and process for preparing it

7. claims: 1-2 (part), 9, 13 (part), 20, 23-26 (part)

compound of formula XIV, its use as a medicament and process for preparing it

8. claims: 1-2 (part), 10-11, 13 (part), 21, 23-26 (part)

compound of formula XV, its use as a medicament and process for preparing it

9. claims: 1-2 (part), 12, 13 (part), 22, 23-26 (part)

compound of formula XVI, its use as a medicament and process for preparing it

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2008/009619

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
GB 1069845	A	24-05-1967	NONE	
US 3479344	A	18-11-1969	NONE	