



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : C07J 41/00, A61K 31/565</p>	<p>A3</p>	<p>(11) International Publication Number: WO 98/24802</p> <p>(43) International Publication Date: 11 June 1998 (11.06.98)</p>
<p>(21) International Application Number: PCT/GB97/03352</p> <p>(22) International Filing Date: 4 December 1997 (04.12.97)</p> <p>(30) Priority Data: 9625334.9 5 December 1996 (05.12.96) GB</p> <p>(71) Applicant (for all designated States except US): IMPERIAL COLLEGE OF SCIENCE TECHNOLOGY AND MEDICINE [GB/GB]; Sherfield Building, Exhibition Road, London SW7 2AZ (GB).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): REED, Michael, John [GB/GB]; Imperial College School of Medicine, St. Mary's Hospital, Unit of Metabolic Medicine, Norfolk Place, Paddington, London W2 1PG (GB). POTTER, Barry, Victor, Lloyd [GB/GB]; University of Bath, Faculty of Science, Dept. of Pharmacy and Pharmacology, Claverton Down, Bath BA2 7AY (GB).</p> <p>(74) Agents: HARDING, Charles, Thomas et al.; D Young & Co., 21 New Fetter Lane, London EC4A 1DA (GB).</p>	<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 27 August 1998 (27.08.98)</p>	
<p>(54) Title: COMPOUND</p>		
<p>(57) Abstract</p> <p>A compound is described. The compound is suitable for use as an inhibitor of oestrone sulphatase. The compound has formula (I); wherein A is a first group; B is an aryl ring structure having at least 4 carbon atoms in the ring and wherein the ring B is substituted in at least the 2 position and/or the 4 position with an atom or group other than H; X is a sulphamate group; wherein group A and ring B together are capable of mimicking the A and B rings of oestrone; and wherein group A is attached to at least one carbon atom in ring B.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 97/03352

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07J41/00 A61K31/565

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 6 C07J 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	DE 44 29 398 A (JENAPHARM GMBH) 15 February 1996	1-19, 28-31
Y	see page 4, line 36 - line 37 see page 5, line 55 - line 64 see page 6, line 6	1-31
X	--- L. WOO ET AL: "Active Site Directed Inhibition of Estrone Sulfatase by Nonsteroidal Coumarin Sulfamates" JOURNAL OF MEDICINAL CHEMISTRY., vol. 39, no. 7, 29 March 1996, WASHINGTON US, pages 1349-1351, XP002059345 see page 1350, column 1; figure 3 see page 1349, column 2 see page 1350, column 2; figure 5 --- -/--	1-5, 10-16, 19,28-31

Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

<p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*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)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p>	<p>*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</p> <p>*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</p> <p>*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.</p> <p>*Z* document member of the same patent family</p>
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Date of the actual completion of the international search 18 June 1998	Date of mailing of the international search report 07.07.98
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Name and mailing address of the ISA 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	Authorized officer Watchorn, P
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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>J. FISHMAN ET AL: "Studies on the Directive O-Methylation of Catechol Estrogens" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY., vol. 89, no. 26, 1967, DC US, pages 7147-7148, XP002059346 see page 7148, column 1, paragraph 1 ---</p>	1-19, 28-31
Y	<p>WO 93 05064 A (IMPERIAL COLLEGE) 18 March 1993 see examples 1-8 ---</p>	1-31
Y	<p>R. PETERS ET AL: "Analogues of [(Triethylsilyl)ethynyl]estradiol as Potential Antifertility Agents" JOURNAL OF MEDICINAL CHEMISTRY., vol. 31, no. 3, 1988, WASHINGTON US, pages 572-576, XP002059347 see page 572, column 2, paragraph 2 see in particular compounds 1,2,4 and 8 see page 574; table II ---</p>	1-19, 28-31
Y	<p>R. RAJAN ET AL: "Estrogen Effects on NADH Oxidase and Superoxide Dismutase in Prepubertal Female Rats" STEROIDS., vol. 40, no. 6, 1982, SAN FRANCISCO US, pages 651-660, XP002059348 see page 654, column 2; table 1 ---</p>	1-19, 28-31
Y	<p>M. CUSHMAN ET AL: "Synthesis, Antitubulin and Antimitotic Activity, and Cytotoxicity of Analogs of 2-Methoxyestradiol, an Endogenous Mammalian Metabolite of Estradiol That Inhibits Tubulin Polymerization by Binding to the Colchicine Binding Site" JOURNAL OF MEDICINAL CHEMISTRY., vol. 38, no. 12, 9 June 1995, WASHINGTON US, pages 2041-2049, XP002059349 see page 2043; table 1 see in particular compounds 1, 8a, 10b, 15 and 23 see page 2045, column 1; table 3 ---</p>	1-19, 28-31
Y	<p>C. LOVELY ET AL: "2-(Hydroxyalkyl)estradiols: Synthesis and Biological Evaluation" JOURNAL OF MEDICINAL CHEMISTRY., vol. 39, no. 9, 26 April 1996, WASHINGTON US, pages 1917-1923, XP002059350 see page 1919; table 2 ---</p>	1-19, 28-31
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International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CHEMICAL ABSTRACTS, vol. 107, no. 21, 23 November 1987 Columbus, Ohio, US; abstract no. 190359, S. BROOKS ET AL: "A-Ring substituted estrogens as inhibitors of the MXT transplantable mammary ductal carcinoma" page 18; column 2; XP002059352 see abstract & CANCER RESEARCH, vol. 47, no. 17, 1987, pages 4623-4629, ---	1-19, 28-31
Y	US 4 668 668 A (BROOKS SAMUEL C ET AL) 26 May 1987 see the whole document ---	1-19, 28-31
Y	TOWNSLEY J D: "Further studies on the regulation of human placental steroid 3-sulfatase activity" ENDOCRINOLOGY, vol. 93, no. 1, 1973, pages 172-181, XP002068155 see page 178, table 6, entry 16 ---	20-31
Y	CHEMICAL ABSTRACTS, vol. 068, no. 1, 1 January 1968 Columbus, Ohio, US; abstract no. 009640, ADAMS J B: "Enzymic synthesis of steroid sulfates. V. Binding of estrogens to estrogen sulfotransferase" page 913; column 2; XP002068156 see abstract & BIOCHIMICA ET BIOPHYSICA ACTA , vol. 146, no. 2, 1967, pages 522-528, ---	20-31
P,X	S. SCHWARZ ET AL: "Synthesis of estrogen sulfamates: Compounds with a novel endocrinological profile" STEROIDS., vol. 61, no. 12, December 1996, SAN FRANCISCO US, pages 710-717, XP002059351 see page 713, compound 9 see page 710, column 1, paragraph 1 -----	1-7, 10-12,19

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 97/ 03352

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. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: 32
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

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. Claims : 1-19, 28-31(partly) Ortho-substituted aryl sulphamate compounds of formula (I), pharmaceutical compositions and uses thereof.
2. Claims : 20-30, 28-31(partly) 17-Unsubstituted estrogen-3-sulphamates of formula (X), pharmaceutical compositions and uses thereof.

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

International Application No. PCT/GB 97/03352

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims Nos.: 32

Claim 32 defines its subject matter by reference to the description and figures, in clear violation of Rule 6.2(a) PCT. In addition this claim qualifies the subject matter to be drawn from the description thus "A sulphamate compound SUBSTANTIALLY as herein described and with reference to any one of figures 2 to 11". The use of the wording "substantially" indicates that not all of the subject matter of the description and figures 2 to 11 is to be construed as being included in this claim, but does not clarify which subject matter is to be included in claim 32 and which is to be excluded. Consequently, the true scope and subject matter of this claim is rendered so unclear according to Article 6 PCT, that no search could be carried out thereon.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. nal Application No

PCT/GB 97/03352

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