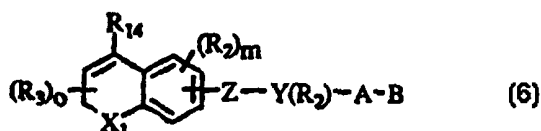
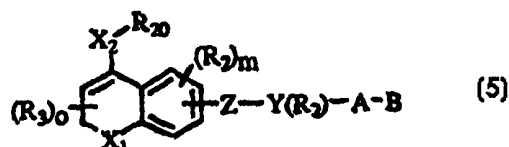
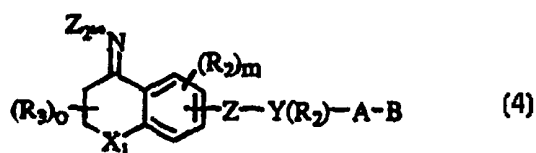
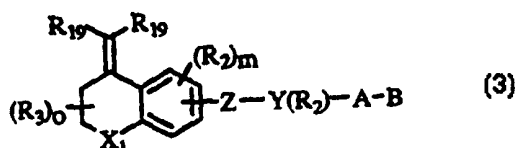
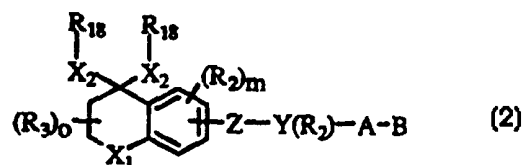
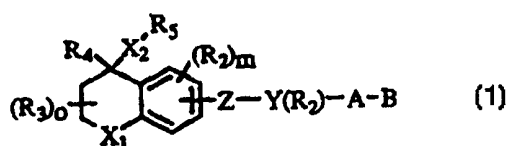




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : C07C 69/587, A61K 31/19, C07C 69/78, 245/10, A61K 31/655, C07C 235/66, C07D 309/12, A61K 31/35</p>	A3	<p>(11) International Publication Number: WO 97/48672</p> <p>(43) International Publication Date: 24 December 1997 (24.12.97)</p>																		
<p>(21) International Application Number: PCT/US97/10725</p> <p>(22) International Filing Date: 19 June 1997 (19.06.97)</p> <p>(30) Priority Data:</p> <table border="0"> <tr><td>08/667,664</td><td>21 June 1996 (21.06.96)</td><td>US</td></tr> <tr><td>08/667,666</td><td>21 June 1996 (21.06.96)</td><td>US</td></tr> <tr><td>08/667,665</td><td>21 June 1996 (21.06.96)</td><td>US</td></tr> <tr><td>08/667,215</td><td>21 June 1996 (21.06.96)</td><td>US</td></tr> <tr><td>08/667,216</td><td>21 June 1996 (21.06.96)</td><td>US</td></tr> <tr><td>08/667,663</td><td>21 June 1996 (21.06.96)</td><td>US</td></tr> </table> <p>(71) Applicant: ALLERGAN [US/US]; 8301 Mars Drive, Waco, TX 76712 (US).</p>		08/667,664	21 June 1996 (21.06.96)	US	08/667,666	21 June 1996 (21.06.96)	US	08/667,665	21 June 1996 (21.06.96)	US	08/667,215	21 June 1996 (21.06.96)	US	08/667,216	21 June 1996 (21.06.96)	US	08/667,663	21 June 1996 (21.06.96)	US	<p>(72) Inventors: VULIGONDA, Vidyasagar, 15 Sweet Rain, Irvine, CA 92714 (US). TENG, Min; 2 Dove Street, Aliso Viejo, CA 92656 (US). BEARD, Richard, L.; 2341 Azure Avenue, Newport Beach, CA 92660 (US). JOHNSON, Alan, T.; 7 Via Arribo, Rancho Santa Margarita, CA 92688 (US). LIN, Yuan; 214 North Goldenrod Drive, Walnut, CA 91789 (US). CHANDRARATNA, Roshantha, A.; 25841 Empresa, Mission Viejo, CA 92691 (US). SONG, Tae, K.; 3768 North Country Club Drive, Long Beach, CA 90807 (US). WONG, Harold, N.; 2 Ceramica, Rancho Santa Margarita, CA 92688 (US). DUONG, Tien, T.; Apartment 15C, 13 Bearpaw, Irvine, CA 92714 (US). GILLET, Samuel, J.; 6125 Hillmont Drive, Oakland, CA 94605 (US).</p> <p>(74) Agents: BARAN, Robert, J. et al.; Allergan, Inc., 2525 Dupont Drive, T-22-E, P.O. Box 19534, Irvine, CA 92623-9534 (US).</p> <p>(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</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: 16 July 1998 (16.07.98)</p>
08/667,664	21 June 1996 (21.06.96)	US																		
08/667,666	21 June 1996 (21.06.96)	US																		
08/667,665	21 June 1996 (21.06.96)	US																		
08/667,215	21 June 1996 (21.06.96)	US																		
08/667,216	21 June 1996 (21.06.96)	US																		
08/667,663	21 June 1996 (21.06.96)	US																		

(54) Title: SUBSTITUTED TETRAHYDRONAPHTHALENE AND DIHYDRONAPHTHALENE DERIVATIVES HAVING RETINOID AND/OR RETINOID ANTAGONIST-LIKE BIOLOGICAL ACTIVITY



(57) Abstract

Compounds of formulas (1-6) where the symbols have the meaning described in the specification, have retinoid and/or retinoid antagonist-like biological activity.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MX	Mexico	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakistan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

INTERNATIONAL SEARCH REPORT

Int ernational Application No PCT/US 97/10725
--

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 6 C07C69/587 A61K31/19 C07C69/78 C07C245/10 A61K31/655
 C07C235/66 C07D309/12 A61K31/35

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 C07C A61K C07D

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.
P, X	WO 97 09297 A (ALLERGAN INC ;KLEIN ELLIOTT S (US); JOHNSON ALAN T (US); STANDEVEN) 13 March 1997 see claims; examples ---	101
P, X	EP 0 736 530 A (SQUIBB BRISTOL MYERS CO) 9 October 1996 see claims; examples ---	101-103, 106, 108
X	EP 0 661 259 A (SQUIBB BRISTOL MYERS CO) 5 July 1995 cited in the application see claims; examples ---	101-108, 116
A	US 5 514 825 A (VULIGONDA VIDYASAGAR ET AL) 7 May 1996 see claims ---	1-120
	-/--	

Further documents are listed in the continuation of box C.

Patent family members are listed in 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

20 May 1998

Date of mailing of the international search report

08/06/1998

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

Sánchez García, J.M.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/10725

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 489 584 A (VULIGONDA VIDYASAGAR ET AL) 6 February 1996 see claims ---	1-120
A	WO 95 33745 A (STANFORD RES INST INT ;JOLLA CANCER RES FOUND (US)) 14 December 1995 see claims; examples ---	1-120
A	D. BONCHEV ET AL: "Modeling the anticarcinogenic action of retinoids by making use of the OASIS method. 3. Inhibition of the induction of ornithine decarboxylase by arotinoids." JOURNAL OF MEDICINAL CHEMISTRY., vol. 37, 1994, WASHINGTON US, pages 2300-2307, XP002063897 see page 2301 ---	1-120
A	JOHNSON A T ET AL: "SYNTHESIS AND CHARACTERIZATION OF A HIGHLY POTENT AND EFFECTIVE ANTAGONIST OF RETINOIC ACID RECEPTORS" JOURNAL OF MEDICINAL CHEMISTRY, vol. 38, no. 24, 24 November 1995, pages 4764-4767, XP000569395 ---	1-120
A	C. AGARWAL ET AL: "AGN193109 is a highly effective antagonist of retionid action in human ectocervical epithelial cells" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 21, 24 May 1996, MD US, pages 12209-1212, XP002063898 see table I ---	1-120
T	JOHNSON, ALAN T. ET AL: "Identification of Retinoic Acid Receptor.beta. Subtype Specific Agonists" J. MED. CHEM. (1996), 39(26), 5027-5030 CODEN: JMCMAR;ISSN: 0022-2623, 1996, XP002065588 see the whole document ---	1-120
A	US 4 539 154 A (KREBS ERNST P) 3 September 1985 see claims ---	1-120
A	WO 96 05165 A (HOFFMANN LA ROCHE ;KLAUS MICHAEL (DE); LOVEY ALLEN JOHN (US); MOHR) 22 February 1996 see claims ---	1-120
7 2	A US 5 324 840 A (CHANDRARATNA ROSHANTHA A S) 28 June 1994 see claims -----	1-120

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No PCT/US 97/10725

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9709297 A	13-03-1997	AU 7235496 A	27-03-1997
EP 0736530 A	09-10-1996	US 5559248 A AU 5050796 A CA 2173047 A JP 8283238 A	24-09-1996 17-10-1996 06-10-1996 29-10-1996
EP 0661259 A	05-07-1995	AT 159010 T AU 8178194 A CA 2138000 A DE 69500813 D DE 69500813 T ES 2107866 T JP 7242591 A US 5648385 A US 5618839 A	15-10-1997 13-07-1995 04-07-1995 13-11-1997 20-05-1998 01-12-1997 19-09-1995 15-07-1997 08-04-1997
US 5514825 A	07-05-1996	AU 4520496 A CA 2208844 A EP 0800517 A WO 9620930 A US 5591858 A	24-07-1996 11-07-1996 15-10-1997 11-07-1996 07-01-1997
US 5489584 A	06-02-1996	AU 4520496 A CA 2208844 A EP 0800517 A WO 9620930 A	24-07-1996 11-07-1996 15-10-1997 11-07-1996
WO 9533745 A	14-12-1995	AU 2823395 A	04-01-1996
US 4539154 A	03-09-1985	NONE	
WO 9605165 A	22-02-1996	AU 3382195 A CA 2196197 A CZ 9700382 A EP 0775103 A FI 970547 A HU 76839 A JP 9512830 T PL 318557 A	07-03-1996 22-02-1996 11-06-1997 28-05-1997 07-02-1997 28-11-1997 22-12-1997 23-06-1997

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No PCT/US 97/10725

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9605165 A		NO 970580 A	07-02-1997
US 5324840 A	28-06-1994	AU 687741 B	05-03-1998
		AU 4525593 A	04-01-1994
		CN 1144091 A	05-03-1997
		EP 0649409 A	26-04-1995
		JP 7508725 T	28-09-1995
		WO 9325530 A	23-12-1993
		US 5475113 A	12-12-1995
		ZA 9303994 A	07-01-1994