



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : A61K 47/48</p>	<p>A3</p>	<p>(11) International Publication Number: WO 98/05362</p> <p>(43) International Publication Date: 12 February 1998 (12.02.98)</p>
<p>(21) International Application Number: PCT/US97/13352</p> <p>(22) International Filing Date: 30 July 1997 (30.07.97)</p> <p>(30) Priority Data: 08/691,617 2 August 1996 (02.08.96) US</p> <p>(71) Applicant: OREX PHARMACEUTICAL DEVELOPMENT CORP. [US/US]; 501 Marford Drive, St. Louis, MO 63141 (US).</p> <p>(72) Inventors: PLATE, Nikolai A.; ul. Zelinskogo, 38-95, Moscow, 117334 (RU). VALUEV, Lev I.; pr. Lokomotivny, 9-a-48, Moscow, 127238 (RU). VALUEVA, Tatyana A.; pr. Lokomotivny, 9-a-48, Moscow, 127238 (RU). STAROSELTSEVA, Ludmila K.; pr. 40 Let Oktjabrja, 15-9, Moscow, 109382 (RU). AMETOV, Alexander S.; ul. akad. Koreleva, 3-a-90, Moscow, 129515 (RU). KNYAZHEV, Vladimir A.; Sokolnichesky val, 40-140, Moscow, 107113 (RU). HENIS, Jay, M., S.; 501 Marford Drive, St. Louis, MO 63141 (US).</p> <p>(74) Agents: SHUST, Nestor, W. et al.; Jones, Day, Reavis & Pogue, North Point, 901 Lakeside Avenue, Cleveland, OH 44114 (US).</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, 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, 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: 7 May 1998 (07.05.98)</p>
<p>(54) Title: PROTEIN-CONTAINING POLYMER COMPOSITION FOR ORAL ADMINISTRATION</p>		
<p>(57) Abstract</p> <p>A therapeutic-containing composition adapted for the oral administration of a biologically active material which comprises a water insoluble but water swellable polymer chemically modified with an enzyme inhibitor containing a chemical functionality which has an interactive affinity for target receptors located on the transport barrier walls of the digestive track of the intended recipient, and at least one therapeutic of low oral bioavailability.</p>		

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			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon	KR	Republic of Korea	PL	Poland		
CN	China	KZ	Kazakhstan	PT	Portugal		
CU	Cuba	LC	Saint Lucia	RO	Romania		
CZ	Czech Republic	LI	Liechtenstein	RU	Russian Federation		
DE	Germany	LK	Sri Lanka	SD	Sudan		
DK	Denmark	LR	Liberia	SE	Sweden		
EE	Estonia			SG	Singapore		

INTERNATIONAL SEARCH REPORT

Intern. Application No
PCT/US 97/13352

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K47/48

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 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 195 10 551 A (INST NEFTECHIMICHESKOGO SINTEZ ;PLATE NIKOLAJ ALFREDOVIC (RU); VAL) 28 September 1995 cited in the application see the whole document	1-13
Y	see page 4, line 20-25; claim 15 ---	1-13
P,X	RU 2 076 733 C (INST NEFTECHIMICHESKOGO SINTEZ) 10 April 1997 see abstract see column 3, paragraph 4-6; examples 1-5 --- -/--	1-13

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

5 March 1998

Date of mailing of the international search report

19.03.98

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

Gonzalez Ramon, N

3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/13352

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>VALUEV L I ET AL: "IMMOBILIZATION OF OVOMUCOID ON DEXTRANS" POLYMER SCIENCE, vol. 34, no. 11, 1 January 1992, pages 972-974, XP000336191 see page 974; table 1 see page 972, column 1</p>	1-13
Y	<p>--- VALUEV L I ET AL: "INTERACTION OF POLYMERIC DERIVATIVES OF TRYPSIN WITH ITS PROTEIN INHIBITOR" POLYMER SCIENCE: SERIE A, vol. 37, no. 9, 1 September 1995, pages 910-914, XP000540705 see abstract; figure 1; table 1 see page 910, column 2</p>	1-13
A	<p>--- WO 95 15352 A (UNIV QUEBEC A MONTREAL) 8 June 1995 see page 24; table 2 see page 25 - page 26; claims 3,4,13,15; figure 6</p>	1-13
Y	<p>--- US 5 049 545 A (LOEBERMANN HARTMUT ET AL) 17 September 1991 cited in the application see abstract see column 2, line 10-24; claim 1; examples 3-6</p>	1-9
A	<p>--- KOPECEK J. ET AL: "Polymers for colon-specific drug delivery" J. CONTROL. RELEASE, 1992, 19/1-3 (121-130), NETHERLANDS, XP002057830 see abstract see page 123 see page 127</p>	1-13
A	<p>--- US 5 359 030 A (EKWURIBE NNOCHIRI N) 25 October 1994 see column 8-9; claims 20,23,31-33 see column 11-12; examples 4,5,7</p>	1-13
A	<p>--- EP 0 098 110 A (JAPAN CHEM RES) 11 January 1984 see page 5; claims 1-3 see page 3</p> <p>-----</p>	1-13

INTERNATIONAL SEARCH REPORT

In international application No.
PCT/US 97/13352

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:
see FURTHER INFORMATION sheet PCT/ISA/210

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:
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.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 97/13352

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

Claims Nos.: 1-4,6-9

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:

In view of the large number of compounds, which are defined by the general definition in the independent claims, the search had to be restricted for economic reasons. The search was limited to the compounds for which pharmacological data was given and/or the compounds mentioned in the claims, and to the general idea underlying the application (see Guidelines, Part B, Chapter III, paragraph 3.6).

Remark : Although claims 11,12 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 compound/composition.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 97/13352

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 19510551 A	28-09-95	RU 2066551 C DK 28795 A US 5698515 A	20-09-96 24-09-95 16-12-97

RU 2076733 C	10-04-97	NONE	

WO 9515352 A	08-06-95	AU 1060495 A EP 0705298 A	19-06-95 10-04-96

US 5049545 A	17-09-91	DE 3604868 A AU 611079 B AU 6879987 A AU 7260091 A DK 73287 A EP 0233600 A JP 62192399 A	20-08-87 06-06-91 20-08-87 30-05-91 16-08-87 26-08-87 22-08-87

US 5359030 A	25-10-94	AU 6946694 A CA 2162366 A EP 0707596 A JP 8510255 T WO 9426778 A US 5438040 A US 5681811 A	12-12-94 24-11-94 24-04-96 29-10-96 24-11-94 01-08-95 28-10-97

EP 0098110 A	11-01-84	JP 58225025 A JP 1784880 C JP 4063053 B JP 59059629 A US 4609546 A	27-12-83 31-08-93 08-10-92 05-04-84 02-09-86
