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(54) Title: VISCOELASTIC AQUEOUS GELS COMPRISING MICROSPHERES

(57) Abstract: The present invention provides viscoelastic gel compositions comprising microparticles which are capable of interacting with each other in a non-ionic manner, thus forming a gel network. The gel compositions may incorporate active agents and provide controlled release of such agents. The compositions are useful as injectable depot formulations of therapeutic compounds. In a further aspect, microparticles capable of gel formation in an aqueous environment are provided, as well as method of making viscoelastic gels based on the interaction of uncharged microparticles. Moreover, the invention discloses kits for making viscoelastic gel compositions and uses thereof.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
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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)
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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, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 183 016 B1 (UNIV UTRECHT [NL]) 21 April 2004 (2004-04-21) paragraphs [0021] - [0075]; claims 1-22; figures 1-9; examples 1,2; tables 1-3	1-65
X	WO 98/22093 A (OCTOPLUS B V [NL]; HENNINK WILHELMUS EVERHARDUS [NL]; FRANSSEN OKKE [N] 28 May 1998 (1998-05-28) abstract; claims 1-9; example 3 ----- -/--	1-65

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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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.
X	WO 2006/071110 A (UNIV UTRECHT [NL]; HENNINK WILHELMUS EVERHARDUS [NL]; VAN DIJK-WOLTHUI) 6 July 2006 (2006-07-06) page 5, line 26 - page 6, line 10 page 8, lines 3-13,24-28 page 10, lines 7-9 page 12, lines 4-6 page 14, lines 29,30 page 15, lines 8-15,25,26 page 16, lines 3-14; claims 3-6,12-23,28-31; figures 1-5,8-10; examples 5-11 -----	1-65
X	WO 98/00170 A (UNIV UTRECHT [NL]; HENNINK WILHELMUS EVERHARDUS [NL]; DIJK WOLTHUIS WE) 8 January 1998 (1998-01-08) page 7, line 24 - page 8, line 12 page 10, lines 26-34; claims 1-8; figures 1-5; examples 2-6 -----	1-65
X	WO 2004/085712 A2 (PENN STATE RES FOUND [US]; LOWE TAO LU [US]; KIM YOUNG SHIN [US]; HUAN) 7 October 2004 (2004-10-07) paragraphs [0034], [0041], [0044], [0054], [0056], [0061], [0063], [0065], [0068], [0085], [0097]; claims 4-6,13,15-18; figures 2-5,7-14 -----	1-65
A	CADEE J A ET AL: "Synthesis, characterization of 2-(methacryloyloxy)ethyl-(di-) l-lactate and their application in dextran-based hydrogels" POLYMER, ELSEVIER SCIENCE PUBLISHERS B.V, GB, vol. 40, no. 24, November 1999 (1999-11), pages 6877-6881, XP004177323 ISSN: 0032-3861 the whole document -----	1-65
A	VAN DIJK-WOLTHUIS W N E ET AL: "A new class of polymerizable dextrans with hydrolyzable groups: hydroxyethyl methacrylated dextran with and without oligolactate spacer" POLYMER, ELSEVIER SCIENCE PUBLISHERS B.V, GB, vol. 38, no. 25, December 1997 (1997-12), pages 6235-6242, XP004092661 ISSN: 0032-3861 the whole document -----	1-65

INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1183016	B1	21-04-2004	EP 1183016 A1	06-03-2002
WO 9822093	A	28-05-1998	AT 322890 T	15-04-2006
			AT 267588 T	15-06-2004
			AU 5069798 A	10-06-1998
			DE 69729312 D1	01-07-2004
			DE 69729312 T2	09-06-2005
			DE 69735688 T2	05-04-2007
			DK 941068 T3	27-09-2004
			EP 0941068 A1	15-09-1999
			ES 2261870 T3	16-11-2006
			ES 2222507 T3	01-02-2005
WO 2006071110	A	06-07-2006	EP 1846457 A1	24-10-2007
WO 9800170	A	08-01-1998	AT 238068 T	15-05-2003
			AU 3360197 A	21-01-1998
			DE 69721265 D1	28-05-2003
			DE 69721265 T2	06-05-2004
			DK 910412 T3	11-08-2003
			EP 0910412 A1	28-04-1999
			ES 2198579 T3	01-02-2004
			JP 2000515853 T	28-11-2000
			PT 910412 T	30-09-2003
WO 2004085712	A2	07-10-2004	NONE	