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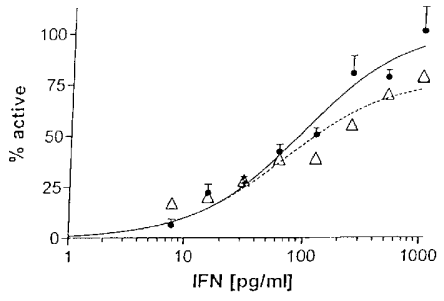
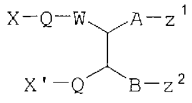
(54) Title: CONJUGATED BIOLOGICAL MOLECULES AND THEIR PREPARATION





(I)

(57) Abstract: Novel biologically active compounds of the general formula (I) in which one of X and X' represents a polymer, and the other represents a hydrogen atom; each Q independently represents a linking group; W represents an electron-withdrawing moiety or a moiety preparable by reduction of an electron-withdrawing moiety; or, if X' represents a polymer, X-Q-W- together may represent an electron withdrawing group; and in addition, if X represents a polymer, X' and electron withdrawing group W together with the interjacent atoms may form a ring; each of Z^1 and Z^2 independently represents a group derived from a biological molecule, each of which is linked to A and B via a nucleophilic moiety; or Z^1 and Z^2 together represent a single group derived from a biological molecule which is linked to A and B via two nucleophilic moieties; A is a C_{1-5} alkylene or alkenylene chain; and B is a bond or a C_{1-4} alkylene or alkenylene chain; are formed by conjugating a suitable polymer to a suitable biologically active molecule via nucleophilic groups in said molecule, preferably via a disulphide bridge.

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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)
IPC 7 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)

EPO-Internal, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WILBUR D SCOTT ET AL: "Monoclonal antibody Fab' fragment cross-linking using equilibrium transfer alkylation reagents. A strategy for site-specific conjugation of diagnostic and therapeutic agents with F(ab')-2 fragments" BIOCONJUGATE CHEMISTRY, vol. 5, no. 3, 1994, pages 220-235, XP002313937 ISSN: 1043-1802 Fig .1; Fig .2, compounds 5a,b -/--	1-14

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
19 January 2005	31/01/2005

Name and mailing address of the ISA	Authorized officer
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	Lopez García, F

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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.
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Y	BROCCHINI ET AL.: "Molecular yardsticks. Synthesis of extended equilibrium transfer alkylating cross-link reagents and their use in the formation of macrocycles" JOURNAL OR THE AMERICAN CHEMICAL SOCIETY, vol. 110, 1988, pages 5211-5212, XP002313940 Scheme I; Scheme II, compounds 12-17 and 32.	1-14
A	WO 99/45964 A (SHEARWATER POLYMERS INC ; HARRIS J MILTON (US); KOZLOWSKI ANTONI (US)) 16 September 1999 (1999-09-16) Abstract; p. 1, l. 11-15; p. 3, l. 18-19; p. 5, l. 1; p. 12, l. 26-p. 13, l. 2; examples; claims 14-20	1-14
A	WO 01/05818 A (KUHNIL PHARM CO LTD ; CHOI JANG SIK (KR); YOON JONG BAE (KR); LEE HYUK) 25 January 2001 (2001-01-25) claim 1.	1-7,13, 14
A	US 2002/103259 A1 (GREENWALD RICHARD B ET AL) 1 August 2002 (2002-08-01) compounds 26, 28, 29, 31, 38, 39.	1-6, 10-14

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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