Title (en)

POTENTIATION OF THE ACTIVATION OF HIGH-MOLECULAR-MASS PRODRUGS

Title (de)

VERSTÄRKUNG DER AKTIVIERUNG VON HOCHMOLEKULAREN PRODRUGS

Title (fr)

POTENTIALISATION DE HAUT POIDS MOLECULAIRE

Publication

EP 1701743 A2 20060920 (FR)

Application

EP 04786328 A 20040819

Priority

- FR 2004002162 W 20040819
- FR 0310114 A 20030822

Abstract (en)

[origin: FR2858936A1] Compound (X) that comprises an agent, active on target cells, linked to a cleavable residue that increases its half-life in the circulation is new. Compounds of formula (A) p-(E-B) n-(I) m (X) are new. I : active compound; A : group that increases half-life of B-I in the circulation; E-B : linking group; B : structure that can be cleaved selectively by an enzyme present only, or preferentially, close to, or at, the target cells; E : hydrophilic spacer, stable in the circulation, which separates A and B so as to permit, or facilitate, cleavage of B close to, or at, the target cells, allowing release of I, optionally together with B; n : integer from 1 to the total number of reactive functional groups of I to which E-B are, or could be, attached; m : integer from 1 to the total number of reactive functional groups on A to which E-B could be attached; and p : integer from 1 to the total number of reactive functional groups of I to which E-B could be attached. Provided that: (1) when p is 1, then n equals m; and (2) when m is 1, then p is 1. ACTIVITY : Cytostatic; Antiinflammatory. Athymic mice carrying a subcutaneous graft of the human colon carcinoma LS-174T were treated with (i) succinyl-beta -Ala-Leu-Ala-Leu-Dox (= doxorubicin) or (ii) poly(ethylene glycol) (PEG) 2000-(D-Ser) 4-Ala-Leu-Ala-Leu-Dox, intravenously, on days 0, 7, 14 and 21. The specific growth delay for (i) was 1.27 (phase 1) and 3.02 (phase 2), for total Dox dose 5 mu mole; for (ii) 0.87 and 1.58, respectively (total Dox dose 3.875 mu mole) and for free Dox (0.669 mu mole; a single dose) 0.53 and 1.86. MECHANISM OF ACTION : None given.

IPC 8 full level

A61K 47/48 (2006.01)

CPC (source: EP)

A61K 47/60 (2017.07); **A61K 47/643** (2017.07); **A61K 47/65** (2017.07); **A61P 43/00** (2017.12)

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