Title (en)

METHODS AND COMPOSITIONS CONTAINING SUCCINIMIDE OR MALEIMIDE DERIVATIVES OF ANTINEOPLASTIC AGENTS, FOR PRODUCING LONG LASTING ANTINEOPLASTIC AGENTS

Title (de)

VERWENDUNGEN UND ZUSAMMENSETZUNGEN, WELCHE SUCCINIMIDE ODER MALEIMIDE DERIVATEN VON ANTINEOPLASTISCHEN WIRKSTOFFEN ENTHALTEN, ZUR HERSTELLUNG ANTINEOPLASTISCHER WIRKSTOFFEN

Title (fr)

METHODES ET COMPOSITIONS COMPRENANTS DES DERIVES SUCCINIMIDIQUES OU MALEIMIDIQUES D'AGENTS ANTINEOPLASTIQUES, DESTINEES A LA PRODUCTION D'AGENTS ANTICANCEREUX A ACTIVITE PROLONGEE

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Application

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Abstract (en)

[origin: WO0117568A2] Methods of and compositions for pulmonary delivery of therapeutic agents which are capable of forming covalent bonds with a site of interest or which have formed a covalent bond with a pulmonary solution protein are disclosed. Therapeutic agents useful in the invention include wound healing agents, antibiotics, anti-inflammatories, anti-oxidants, anti-proliferatives, immunosupressants, anti-infective and anti-cancer agents.

[origin: WO0117568A2] In order to meet these needs, the present invention is directed to therapeutic and diagnostic agents capable of forming covalent bonds to blood and pulmonary fluid proteins or other components ex vivo or in vivo. The therapeutic agents of this invention have a long duration of action for the management of disease. The invention relates to ex vivo and in vivo bioconjugation of therapeutic agents to protein (e.g. albumin), as well as an intrapulmonary in vivo bioconjugation of therapeutic agents to endogenous pulmonary fluid proteins or other components to dramatically increase the half life of the therapeutic agents and avoid the need for parenteral administration. This invention is further directed to the use of reactive chemistries including: N-hydroxy sulfosuccinimide, maleimide-benzoyl-succinimide, gamma-maleimido-butyryloxy succinimide ester, maleimidopropionic acid, isocyanate, thiolester, thionocarboxylic acid ester, imino ester, and carbodiimide anhydride. Maleimidopropionic acid is the preferred reactive chemistry, but the invention also contemplates the selection of the above and like reactive chemistries as an electrophilic moeity for bioconjugations with albumin or other proteins. Modified therapeutic agents mentioned are the anti-histamine drug loratidine or cetirizine, a hypothyroid drug, the anti-angina drug tirofiban, the anti-hypertensive drug enalapril, the anti-arrhytmic drug capobenic acid, the antidepressant drug fluoxetine, the bronchodilation drug the obromineacetamine, the antiinflammatory drug loxoprofen, the anti-thyroid deficiency drug thyroxin, and 4-anilino-1-(2-phenethyl)piperidine.

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