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Boratyński et al.

(54) METHOD OF PRODUCTION OF POLYANIONIC DRUG-CARRIER CONJUGATES

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(56) **References Cited**

FOREIGN PATENT DOCUMENTS

WO WO 2004/052406 A1 6/2004

OTHER PUBLICATIONS

Endo et al. 1987; In vitro cytotoxicity of a human serum albuminmediated conjugate of methotrexate with anti-MM46 monoclonal antibody. Cancer Research. 47: 1076-1080.*

Kosasih et al. 2000; Characterization and in vitro release of methotrexate from gelatin/methotrexate conjugates formed using different preparation variables. International Journal of Pharmaceuticals. 204: 81-89.*

Sigma-Aldrich, 2013. Buffer Reference Center. www.sigmaaldrich. com/life-science/core-bioreagents/biological-buffers.*

International Search Report issued by the International Searching Authority (ISA/O.E.P.M.) on Sep. 6, 2010 in connection with International Application No. PCT/PL2009/050031.

* cited by examiner

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(57) **ABSTRACT**

The invention concerns the method of production of a polyanionic macromolecule which is a protein built, among others, from polar amino acids such as lysine, arginine, aspartic acid, glutamic acid), characteristic in that, as a result of the reaction between amine groups and the cyclic anhydride of dicarboxylic acid, the charge changes towards more negatively charged carrier. This reaction gives rise to better therapeutic properties of macromolecules modified in this way.

2 Claims, No Drawings