药学学报 1996, 31(8) 632-636 DOI: ISSN: CN:

论文

单克隆抗体—表阿霉素免疫偶合物的制备和体外活性

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摘要：

用双功能试剂己二酰肼制备腙键连接的聚谷氨酸—表阿霉素,通过控制交联条件,所得产物克服了大分子自身交联的缺点,交联率较高。聚谷氨酸的载药量与分子量呈正比,平均每8～11个谷氨酸单体连接1分子表阿霉素。分子量为14300的聚谷氨酸做载体其载药量为1:11,与单抗交联所得的偶合物McAb:PGA:PAR为1:2:22。偶合物较好地保留了抗体活性,体外细胞毒性较游离药物略有下降,但表现出单抗介导的靶细胞选择性杀伤作用。本研究用腙键交联法成功地制备了药/抗比高且体外有效的免疫偶合物,为进一步制备细胞靶向的肿瘤化疗制剂奠定了基础。

关键词： 表阿霉素 聚谷氨酸 单克隆抗体 免疫偶合物 靶向作用

PREPARATION AND *IN VITRO* ACTIVITY OF MONOCLONAL ANTIBODY-PHARMORUBICIN IMMUNOCONJUGATES

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Abstract:

Bifunctional agent adipic dihydrate was used to form hydrazon bond between polyglutamic acid (PGA) and pharmorubicin (PAR). Under controlled condition, a relatively high rate of conjugation was obtained with no self-condensation. The value of PGA/PAR was in positive portion with the molecular weight (MW) of PGA: per 8～11 glutamic acid monomer linking one pharmorubicin. When PGA of MW 14 300 was used as carrier, the ratio of PGA/PAR was 1:11. After conjugating with anti-hepatoma monoclonal antiboty (McAb), an immunoconjugate of McAb:PGA:PAR being 1:2:22 was obtained. The immunoconjugate retained the binding activity to targeted cell compared with the purified and the oxidized antibody. Pharmacological studies *in vitro* showed lower cytotoxicity of the immunoconjugate than the free drug, but selective cytotoxicity directed by antibody was observed. Consequently, the immunoconjugate McAb-PGA-PAR with high ratio of drug/McAb as well as moderate targeting cytotoxity *in vitro* was successfully prepared. That makes it possible for the preparation of cell targeted drug which is expected to be benificial to tumor treatment.

Keywords: Polyglutamic acid Monoclonal antibody Immunoconjugate Targeting cytotoxity Pharmorubicin

收稿日期 1995-09-04 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者:

作者简介:

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