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论文

靶向肿瘤新生血管的阿霉素阳离子脂质体的体外研究

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摘要：

本研究采用3β-［N-(N′,N′-二甲基胺乙基)胺基甲酰胺基］胆固醇(DC-Chol)和二棕榈酰磷脂酰胆碱为脂材制备了各种DC-Chol含量不同的阿霉素阳离子脂质体，考察了阿霉素阳离子脂质体的体外性质，同时以大鼠主动脉内皮细胞为模型，考察它们对不同阳离子脂质体的摄取情况，并采用静脉注射FITC-Dextran(M_r 500 000)标记体内肿瘤新生血管，为体内靶向肿瘤血管提供依据。结果表明阿霉素阳离子脂质体包封率均在90%以上，粒径在100~200 nm。随着DC-Chol含量的增加，zeta电位升高，但PEG的加入会降低zeta电位。DC-Chol含量的增加会增大阿霉素的释放量，同时也促进脂质体被内皮细胞的摄取，加快摄取速度。因此在进行体内靶向肿瘤血管考察时应充分关注这些体外实验结果。FITC-Dextran标记法可以显影体内新生血管，为体内肿瘤血管靶向实验提供直观的观察方法。

关键词： 肿瘤新生血管靶向 阳离子脂质体 阿霉素 内皮细胞

Cationic liposomes loaded with doxorubicin targeting to the tumor neovasculature in vitro

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Abstract:

This study was conducted to investigate the in vitro characteristics of cationic liposomes composed of 3β-［N-［2-(N′,N′-dimethylamino)ethyl］ carbamoyl］ cholesterol (DC-Chol) and dipalmitoylphosphatidylcholine loaded with doxorubicin (DXR), and to provide useful information for the in vivo tumor vascular targeting of cationic liposomes. Cationic liposomes composed of different amounts of DC-Chol (0 mol%, 10 mol%, 25 mol%, 50 mol%) were loaded with the conventional anti-cancer drug doxorubicin. Their size, zeta potential, encapsulation efficiency, and DXR release in vitro were investigated. Moreover, their uptake by rat aortic endothelial cells (RAECs) was observed at 15 min, 30 min, 1 h, and 4 h of incubation. FITC-Dextran was iv injected to the H22 tumor-bearing KM mice to stain the neovasculature. The characteristics of resulting DXR-loaded cationic liposomes were in stable characteristics with particle sizes around 100-200 nm and capsulation efficiency greater than 90%. Increased cationic lipid led to enhanced zeta potential, and meanwhile it also resulted in quick release of the loaded drug, indicating increased slits or pores on the membrane upon the addition of DC-Chol. RAECs could more avidly take up DXR-loaded cationic liposomes when the content of DC-Chol increased in the liposomes, and DXR were quickly released in the cytoplasm and transported to the nuclei. The neovasculature stained by FITC-Dextran was clearly observed. DXR-cationic liposomes composed of DC-Chol could be used for tumor vascular targeting in vivo for further study.

Keywords: cationic liposome doxorubicin endothelial cell tumor vascular targeting

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