基于环糊精自组装的超支化聚轮烷抗癌药物载体的研究

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本文研究了具有超支化结构的聚轮烷-阿霉素药物载体的制备及其抗肿瘤作用。通过一系列的化学反应及环糊精与PEG的主客体自组装过程方法成功制备了pH敏感的阿霉素药物偶联载体，实验结果表明该制备方法具有分子量可控，分子量分布窄，载药量固定等优点，且合成的药物载体生物相容性较好。通过动态光散射（DLS）及透射电镜（TEM）发现，该药物载体可以在水溶液中进一步自组装形成粒径在100 nm左右的均一纳米粒子。体外释放研究表明，由于药物阿霉素是通过酸敏感的腙键与聚轮烷相连，药物阿霉素在pH=6及pH=5的释放情况下明显快于人体血液生理pH=7.4的释放情况，达到了刺激响应性释放的目的。体外研究表明，该药物偶联载体对肺癌细胞株A549的体外增殖有明显的抑制作用，其效果要好于单纯的阿霉素；通过考察药物偶联载体对S180 荷瘤小鼠的生长影响，进一步评价偶联药物载体抗肿瘤效果，结果表明，超支化的聚轮烷-阿霉素偶联药物载体对S180 荷瘤小鼠的肿瘤生长有明显抑制作用且对小鼠的毒副作用明显小于单纯的药物阿霉素。

关键词：环糊精；聚轮烷；药物载体；阿霉素

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pH-Responsive Dendritic Polyrotaxane drug-polymer conjugates forming nanoparticles as efficient drug delivery system for cancer therapy

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In this study, we have successfully prepared a kind of pH-responsive dendritic polyrotaxane drug-polymer conjugates (PR-*g*-DOX). The dynamic laser scattering (DLS) and transmission electron microscope (TEM) studies demonstrated the conjugates self-assembled into nanoparticles in aqueous solution with globular morphology and compact nanoparticles with diameter around 100 nm. The nanoparticles could rapidly release the drugs in a relatively mildly acidic environment. The conjugates showed prior anticancer effects to the cancer cell lines A549 compared with free DOX. In vivo results revealed the better drug tolerability of the PR-*g*-DOX nanoparticles and a higher in vivo efficacy without increasing its toxicity of the PR-*g*-DOX nanoparticles. It is believed that more potential applications will be possible based on the outstanding properties of the conjugates nanoparticles.