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A novel Doxorubicin loaded folic acid conjugated PAMAM modified with borneol, a nature dual-functional product of reducing PAMAM toxicity and boosting BBB penetrationFanzhu Li¹, XiuLing Xu¹, JingJing Li¹, ShunPing Han¹, ChengHao Tao¹, Luo Fang¹, Yue Sun¹, JiaZhen Zhu¹ and ZeHua Liang¹¹Zhejiang Chinese Medical University, China²Zhejiang Cancer Hospital, China

Effective targeting drug delivery system for glioma treatment is still greatly challenged by the existence of the blood-brain barrier (BBB) and the intracranial over spreading of anti-tumor drug. Herein, we presented a dual-functional glioma targeting delivery of Doxorubicin based on the PAMAMG5 dendrimer, modified with folic acid (FA) to target tumor cell, also borneol (BO), a well-known safe material derived from traditional Chinese medicine, to facilitate the BBB permeability and reduce the toxicity of naked PAMAM. The intracranial transportation and glioma targeting ability were evaluated on the BBB model and C6 glioma cells *in vitro*. Also, pharmacokinetics and bio-distribution were studied on C6 glioma-bearing rats *in vivo*. It indeed reduced the cytotoxicity of PAMAM against both HBMEC and C6 cells by coupling BO on the surface, while efficiently boosted BBB permeability with the improvement of transportation ratio by two folds to the BO-unmodified conjugates. Furthermore, conjugated FA increased total uptake amount by C6 cells leading to strong inhibition with the three-fold lower IC₅₀ value than FA-unmodified DOX conjugate. In comparison with DOX solution, FA-BO-PAMAM/DOX exhibited significantly prolonged half-life time and increased area under the curve and improved DOX accumulation in brain tumor. The tumor growth inhibition, *in vivo*, was significantly increased up to 57.4%. The median survival time of xenograft rats after administering FA-BO-PAMAM/DOX (28 days) was significantly prolonged compared to free DOX (18 days, P<0.05) or other controls. In conclusion, this strategy of novel targeting nanocarrier provides a promising method to increase the drug accumulation in the tumor site for therapy of glioma.

Biography

Fanzhu Li is a Doctor, Professor, Doctoral Supervisor and Post-doctoral Cooperative Tutor. In March 2002, he was introduced as a special talent to Zhejiang Chinese Medical University. Now, he is Dean of College of Pharmaceutical Science. He engaged in novel drug delivery system, targeting preparation, new dosage form and novel technique as well as the process of Chinese medicine *in vivo* for a long time. At the same time, he has established targeted drug delivery systems of brain, liver, kidney and other organs, studied new methods of administration of nasal mucosa, and first initiated a new model of the process of traditional Chinese medicine *in vivo* in china.

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