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Cationic Solid Lipid Nanoparticles Conjugated with Anti-Melantransferrin and Apolipoprotein E for Delivering Doxorubicin to U87MG Cells

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Abstract : Cationic solid lipid nanoparticles (CSLNs) with anti-melanotransferrin (AMT) and apolipoprotein E (ApoE) were used to carry antimitotic doxorubicin (Dox) across the blood–brain barrier (BBB) for glioblastoma multiforme (GBM) treatment. Dox-loaded CSLNs were prepared in microemulsion, grafted covalently with AMT and ApoE, and applied to human brain microvascular endothelial cells (HBMECs), human astrocytes, and U87MG cells. Experimental results revealed that an increase in the weight percentage of stearyl amine (SA) from 0% to 20% increased the size of AMT-ApoE-Dox-CSLNs. In addition, an increase in the stirring rate from 150 rpm to 450 rpm decreased the size of AMT-ApoE-Dox-CSLNs. An increase in the weight percentage of SA from 0% to 20% enhanced the zeta potential of AMT-ApoE-Dox-CSLNs. Moreover, an increase in the stirring rate from 150 rpm to 450 rpm reduced the zeta potential of AMT-ApoE-Dox-CSLNs. AMT-ApoE-Dox-CSLNs exhibited a spheroid-like geometry, a minor irregular boundary deviating from spheroid, and a somewhat distorted surface with a few zigzags and sharp angles. The encapsulation efficiency of Dox in CSLNs decreased with increasing weight percentage of Dox and the order in the encapsulation efficiency of Dox was 10% SA > 20% SA > 0% SA. However, the reverse order was true for the release rate of Dox, suggesting that AMT-ApoE-Dox-CSLNs containing 10% SA had better-sustained release characteristics. An increase in the concentration of AMT from 2.5 to 7.5 μg/mL slightly decreased the grafting efficiency of AMT and an increase in that from 7.5 to 10 μg/mL significantly decreased the grafting efficiency. Furthermore, an increase in the concentration of ApoE from 2.5 to 5 μg/mL slightly reduced the grafting efficiency of ApoE and an increase in that from 5 to 10 μg/mL significantly reduced the grafting efficiency. Also, AMT-ApoE-Dox-CSLNs at 10 μg/mL of ApoE could slightly reduce the transendothelial electrical resistance (TEER) and increase the permeability of propidium iodide (PI). An incorporation of 10 μg/mL of ApoE could reduce the TEER and increase the permeability of PI. AMT-ApoE-Dox-CSLNs at 10 μg/mL of AMT and 5-10 μg/mL of ApoE could significantly enhance the permeability of Dox across the BBB. AMT-ApoE-Dox-CSLNs did not induce serious cytotoxicity to HBMECs. The viability of HBMECs was in the following order: AMT-ApoE-Dox-CSLNs = AMT-Dox-CSLNs = Dox-CSLNs > Dox. The order in the efficacy of inhibiting U87MG cells was AMT-ApoE-Dox-CSLNs > AMT-Dox-CSLNs > Dox-CSLNs > Dox. A surface modification of AMT and ApoE could promote the delivery of AMT-ApoE-Dox-CSLNs to cross the BBB via melanotransferrin and low density lipoprotein receptor. Thus, AMT-ApoE-Dox-CSLNs have appropriate physicochemical properties and can be a potential colloidal delivery system for brain tumor chemotherapy.

Keywords : anti-melanotransferrin, apolipoprotein E, cationic catanionic solid lipid nanoparticle, doxorubicin, U87MG cells
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