

论文

血栓靶向尿激酶脂质体的制备及其体内溶栓效果

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摘要:

目的制备血栓靶向的尿激酶脂质体,并在大鼠颈总动脉血栓模型上考察其溶栓情况。方法通过液相合成法合成出靶向于血栓的特异性配体H-Arg-Gly-Asp-Ser-OH (RGDS),并将其与monocarboxyl poly (ethylene glycol) 3 500 distearoyl phosphatidylethanolamine (DSPE-PEG_{3 500}-COOH)偶联后插入到脂质体双层膜中得到血栓靶向尿激酶脂质体;通过制备方法的改进,以氢化豆磷脂在室温下制备尿激酶脂质体;在大鼠颈总动脉血栓模型上,考察了血栓靶向脂质体的体内溶栓效果。结果所得的尿激酶脂质体包封率高、粒径小,稳定性好;与空白对照组的栓重相比,在相同剂量(60 kU·kg⁻¹,小剂量)下,游离尿激酶组几乎无任何改变,尿激酶脂质体组血栓重量稍有减轻但无显著性差异,血栓靶向尿激酶脂质体组血栓重量明显减轻(P<0.001);干重时的情况略有不同。与同剂量的普通脂质体相比,血栓靶向尿激酶脂质体溶栓效果显著改善(湿重时P<0.01,干重时P<0.05),表现出明显的靶向溶栓能力。结论所制备的血栓靶向尿激酶脂质体具有靶向溶栓的效果。

关键词: 血栓靶向 RGDS 尿激酶 脂质体 颈总动脉血栓模型

Preparation of thrombus-targeted urokinase liposomes and its thrombolytic effect in model rats

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Abstract:

AimTo prepare thrombus-targeted urokinase liposomes and observe its improved thrombolytic efficacy on thrombus model rats. MethodsThe ligand H-Arg-Gly-Asp-Ser-OH (RGDS) which has specific affinity to thrombus was synthesized by liquid phase method and anchored on the surface of liposomes by incorporating its conjugate with DSPE-PEG_{3 500}-COOH into liposomal lipid bilayers, thus thrombus-targeted liposomes were produced. Urokinase (UK) liposomes were prepared at room temperature through method modification using hydrogenated soy phosphatidylcholine (HSPC); the *in vivo* thrombolysis of the obtained thrombus-targeted UK liposomes and its comparison with TBS (Tris-HCl buffered solution) control, free UK and UK liposomes were assessed on common carotid artery model rats. ResultsThe obtained liposomes were characteristic of high UK entrapment efficiency, small mean diameter and good storage stability. At the same dose (60 000 U·kg⁻¹), compared to the wet thrombi weights of TBS control group, those of free UK group and UK liposome group showed no statistical difference, while those of targeted UK liposomes group were significantly decreased (P<0.001); when evaluated in term of dry thrombi weights the result was slightly different. Compared to UK liposomes of the same dose, the targeted UK liposomes showed significantly improved thrombolytic efficacy (P<0.01 in wet weights decrease and P<0.05 in dry weights decrease respectively). ConclusionThe targeted UK liposomes displayed good targeted thrombolytic effect.

Keywords: RGDS urokinase liposomes common carotid artery thrombus model thrombus-targeted

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