

论文

9-硝基喜树碱在Caco-2细胞模型中的体外摄取、转运及外排动力学

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摘要:

目的研究9-硝基喜树碱(9-NC)的细胞摄取、转运及外排特性。方法一种体外培养的人小肠上皮细胞模型Caco-2应用于9-NC的小肠上皮细胞的摄取、跨膜转运及外排动力学研究。评价了时间、温度、pH、P-糖蛋白(P-glycoprotein, P-gp)抑制剂对细胞摄取的影响。采用HPLC测定药物含量。结果9-硝基喜树碱以被动扩散为主要方式被细胞摄取和转运。药物的摄取与时间呈正相关,与温度、pH呈负相关。P-gp抑制剂环孢菌素和维拉帕米增加9-NC细胞摄取(P<0.05)。药物从Basolateral(B,基底面)到Apical(A,肠腔面)的渗透系数P_{app}大于A到B(2.6-6.9倍)。9-NC外排符合二级外排动力学过程,A侧m₀ [(148.0±2.2) pmol·cm⁻²]和外排速率(41.1 pmol·cm²·min⁻¹)高于B侧的m₀ [(121±7) pmol·cm⁻² (P<0.05)和外排速率(29.2 pmol·cm²·min⁻¹)(P<0.01)。结论 9-NC是以被动扩散方式为主要方式被小肠上皮细胞摄取和转运,并受到P-糖蛋白强烈的外排作用。

关键词: 9-硝基喜树碱 Caco-2细胞 摄取 P-糖蛋白 跨膜转运 外排动力学

The *in vitro* kinetics of uptake, transport and efflux of 9-nitrocamptothecin in Caco-2 cell model

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Abstract:

AimTo study the kinetics of uptake, transepithelial transport and efflux of 9-nitrocamptothecin (9-NC). MethodsA human intestinal epithelial cell model Caco-2 cell *in vitro* cultured had been applied to study the kinetics of uptake, transport and efflux kinetics of 9-NC at small intestine. The effects of time, pH, temperature and P-glycoprotein inhibitors on the uptake of 9-NC were investigated. The determination of 9-NC was performed by HPLC. ResultsThe uptake and absorption of 9-NC were passive diffusion as the dominating process. The uptake of 9-NC is positively correlated to uptake time, and negatively correlated to pH and temperature. The inhibitors, cyclosporine A and verapamil, significantly enhanced the uptake amount of 9-NC (P<0.05). P_{app} of Basolateral to Apical was much more than that of Apical to Basolateral (2.6-6.9 fold). The efflux of 9-NC was fitted to apparent two-order process. The m₀ [(148.0±2.2) pmol·cm⁻²] and the efflux rate (41.1 pmol·cm²·min⁻¹) on Apical side were higher than the m₀ [(121±7) pmol·cm⁻²] (P<0.05) and the efflux rate (29.2 pmol·cm²·min⁻¹) on Basolateral side (P<0.01). ConclusionThe uptake and absorption of 9-NC were passive diffusion as the dominating process. P-glycoprotein had strong efflux effects on the uptake and transepithelial transport of 9-NC.

Keywords: Caco-2 cell uptake P-glycoprotein transepithelial transport efflux kinetics 9-nitrocamptothecin

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