

论文

普朗尼克抑制P-糖蛋白药泵的作用

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摘要:

采用Caco-2细胞和动物模型,以维拉帕米为阳性对照,考察普朗尼克对塞利洛尔在Caco-2单层膜与肠道黏膜吸收的影响。用高效液相色谱法检测药物浓度,计算表观透过系数、吸收速率常数与有效透过系数等参数,评价普朗尼克对P-糖蛋白药泵的抑制作用。结果显示,塞利洛尔Caco-2细胞膜转运基底端(BL)到顶端(AP)的透过系数 P_{app} 大于AP到BL的 P_{app} ,分别为 $(2.10 \pm 0.13) \times 10^{-6}$ 和 $(0.333 \pm 0.018) \times 10^{-6} \text{ cm} \cdot \text{s}^{-1}$,且双向转运受到抑制剂维拉帕米和普朗尼克的影响。大鼠在体肠灌注实验中塞利洛尔在十二指肠段、空肠、回肠与结肠段的吸收速率常数 k_a 分别为 (0.09 ± 0.03) , (0.14 ± 0.04) , (0.11 ± 0.03) 与 $(0.05 \pm 0.02) \text{ h}^{-1}$;合用维拉帕米后各肠段吸收速率常数 k_a 分别为 (0.14 ± 0.03) , (0.24 ± 0.02) , (0.25 ± 0.03) 和 $(0.23 \pm 0.02) \text{ h}^{-1}$;合用普朗尼克后各肠段吸收速率常数 k_a 分别为 (0.13 ± 0.02) , (0.22 ± 0.02) , (0.22 ± 0.03) 和 $(0.20 \pm 0.03) \text{ h}^{-1}$ 。可见,普朗尼克通过抑制P-gp外排作用,促进塞利洛尔Caco-2细胞膜和大鼠肠道黏膜的吸收。

关键词: Caco-2细胞模型 P-糖蛋白 在体肠灌注 塞利洛尔 普朗尼克

The inhibitory effect of Pluronic on P-glycoprotein drug pump

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Abstract:

To investigate the inhibitory effect of Pluronic on P-glycoprotein (P-gp) drug efflux pump, Caco-2 cells and animal models were established to study the influence of Pluronic on celiprolol transport across Caco-2 cell monolayer and intestinal mucous membrane with verapamil set as a positive control. Drug concentration was measured by HPLC and the apparent permeability coefficient (P_{app}), absorption rate constant (k_a) and the effective permeability coefficient (P_{eff}) were calculated. P_{app} of basolateral to apical side and apical to basolateral side was $(2.10 \pm 0.13) \times 10^{-6}$ and $(0.333 \pm 0.018) \times 10^{-6} \text{ cm} \cdot \text{s}^{-1}$, respectively. Transports of celiprolol across Caco-2 cell monolayer were influenced by both verapamil and Pluronic. The absorption constants (k_a) of celiprolol at duodenum, jejunum, ileum, and colon were (0.09 ± 0.03) , (0.14 ± 0.04) , (0.11 ± 0.03) and $(0.05 \pm 0.02) \text{ h}^{-1}$, k_a of celiprolol in verapamil group were (0.14 ± 0.03) , (0.24 ± 0.02) , (0.25 ± 0.03) and $(0.23 \pm 0.02) \text{ h}^{-1}$, and k_a of celiprolol in Pluronic group were (0.13 ± 0.02) , (0.22 ± 0.02) , (0.22 ± 0.03) and $(0.20 \pm 0.03) \text{ h}^{-1}$, respectively. Pluronic showed significant effect on inhibiting P-gp of Caco-2 cell and intestinal mucosa in rats.

Keywords: P-glycoprotein *in situ* intestinal perfusion celiprolol Pluronic Caco-2 cell model

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