

论著

小鼠灌胃鬼臼树脂表观体内残留量动力学

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摘要 目的 测定小鼠灌胃给药鬼臼树脂表观体内残留量动力学参数, 为临床合理用药提供依据。方法 采用 Bliss法评定鬼臼树脂的急性毒性。小鼠270只分成9组, 每只小鼠给药2次, 按5, 10, 15, 30, 60 min, 2, 4, 8和12 h序设置各组给药间隔。首次给药量为 $160 \text{ mg} \cdot \text{kg}^{-1}$, 第2次给药剂量动态调整 ($160 \sim 240 \text{ mg} \cdot \text{kg}^{-1}$) 使累积死亡率控制在20%~80%之间; 根据每组小鼠累积死亡数计算鬼臼树脂的表观药动学参数。结果 鬼臼树脂灌胃给药的 LD_{50} 为 $307.4 \text{ mg} \cdot \text{kg}^{-1}$ 。体内过程属开放一室模型; 主要表观药动学参数如下: k_e 为 0.1844 h^{-1} , $t_{1/2ke}$ 为 3.7573 h , k_a 为 1.2579 h^{-1} , $t_{1/2ka}$ 为 0.5509 h , t_{\max} 为 1.6048 h , A_{mas}/F 为 $115.0 \text{ mg} \cdot \text{kg}^{-1}$ 。结论 本方法适合鬼臼树脂的药代动力学评价, 测定结果为临床合理用药提供了依据。

关键词 鬼臼树脂 小鼠 急性死亡率法 药代动力学

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Apparent pharmacokinetics of intragastric administration of podophyllin in mice

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Abstract

AIM To determine the apparent residual dose kinetic parameters of ig podophyllin in mice for rational use of the drug. **METHODS** Acute toxicity of podophyllin was evaluated by Bliss method. Two hundreds and seventy mice were divided into nine groups. Every mouse was administrated twice, the first dose of podophyllin was $160 \text{ mg} \cdot \text{kg}^{-1}$ and the second was an adjusted dosage ($160 \sim 240 \text{ mg} \cdot \text{kg}^{-1}$) to make the mortality of mice between 20%~80% and the time interval of administration was 5, 10, 15, 30, 60 min, 2, 4, 8 and 12 h, respectively. According to the mortality of mice apparent pharmacokinetics parameters were calculated. **RESULTS** LD_{50} of ig podophyllin was $307.4 \text{ mg} \cdot \text{kg}^{-1}$. Pharmacokinetics of podophyllin could be described by the one compartment open model. The main apparent pharmacokinetic parameters of podophyllin were as follows: $k_e = 0.1844 \text{ h}^{-1}$, $t_{1/2ke} = 3.7573 \text{ h}$, $k_a = 1.2579 \text{ h}^{-1}$, $t_{1/2ka} = 0.5509 \text{ h}$, $t_{\max} = 1.6048 \text{ h}$. $A_{\text{mas}}/F = 115.0 \text{ mg} \cdot \text{kg}^{-1}$. **CONCLUSION** The method can be used in pharmacokinetic study of podophyllin and the data are of benefit for rational use of the drug.

Key words

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