

论文

奥沙利铂的水合反应及其酸度的影响

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摘要:

目的研究不同温度时奥沙利铂的水合反应以及酸度的影响, 获得相关的动力学数据, 为临床用药提供指导。方法用电导法和高效液相色谱法测定反应体系中反应物随时间变化情况。结果奥沙利铂的水合反应遵循一级反应的规律, 在水溶液介质中不加 $H^+$ 时,  $25\text{ }^\circ\text{C}$ 下其水合反应的表观速率常数 $k_{\text{obs}}=7.76\times 10^{-6}\cdot\text{min}^{-1}$ , 半衰期 $t_{1/2}=62\text{ d}$ ; 当加入 $H^+$ 时, 水合反应的表观速率常数随 $H^+$ 浓度的增加而增大, 且有 $k_{\text{obs}}=(2.61+21.9 [H^+])\times 10^{-4}\cdot\text{min}^{-1}$ 。提出了水合反应机理, 并由此推导出不加 $H^+$ 时奥沙利铂水合反应速率方程为 $r=(k_1 k_2) [L\text{-OHP}] /k-1$ , 加入 $H^+$ 则速率方程为 $r=(k_1 + k_0 k_3 [H^+]) [L\text{-OHP}]$ , 与试验结果相吻合。结论奥沙利铂的水溶液比较稳定, 符合临床用药的要求。

关键词: 奥沙利铂 水合反应 一级反应 反应机理

The aquation of oxaliplatin and the effect of acid

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Abstract:

Aim To investigate the aquation of oxaliplatin in aqueous solution at different temperatures and gain the kinetic data. Methods Electronic conductometry and high performance liquid chromatography (HPLC) were used to measure the oxaliplatin content in the reaction systems at different time. Results The aquation of oxaliplatin followed a pseudo-first-order rate law. In the absence of  $H^+$ , the observed rate constant  $k_{\text{obs}}$  was  $7.76\times 10^{-6}\cdot\text{min}^{-1}$  and the half life  $t_{1/2}$  was 62 days at  $25\text{ }^\circ\text{C}$ . In the presence of  $H^+$ , the aquation could be accelerated by  $H^+$  according to the equation  $k_{\text{obs}}=(2.61+21.9 [H^+])\times 10^{-4}\cdot\text{min}^{-1}$ . The mechanism of aquation has also been proposed in this paper. From the mechanism, the rate of aquation following to  $r=(k_1 k_2) [L\text{-OHP}] /k-1$  in the absence of  $H^+$  and  $r=(k_1 + k_0 k_3 [H^+]) [L\text{-OHP}]$  in the presence of  $H^+$  have been deduced, which were in perfect agreement with the experimental results. Conclusion In the absence of  $H^+$ , the aqueous solution of oxaliplatin is stable, which meets to the request of clinical.

Keywords: aquation the first-order reaction reaction mechanism oxaliplatin

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