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THE PHARMACOKINETIC STUDIES OF PROMETHAZINE IN RATS PLASMA UNDER THE
SIMULATED MICROGRAVITY CONDITION**Abstract**

Promethazine Hydrochloride (PH) is a kind of medicines used to deal with space motion sickness (SMS) by National Aeronautics and Space Administration (NASA) during manned flight in 1988. Microgravity may affect the change process such as absorption, distribution, metabolism and excretion of the drug inside the organism, which may lead to changes in the efficacy of astronauts in the space environment, and even produce toxic side effects. This paper aimed at to compare pharmacokinetics (PK) of PH in rats plasma after intramuscular administration between normal and different tail-suspended cycles. PH in rat plasma was determined by the fully-validated HPLC-MS method with Loratadine as internal standard and subjected to pharmacokinetics analysis. There were two peaks in stimulated microgravity. The parameters of rats which were tail-suspended for 3 days and 7 days were significantly decreased to those of normal group $AUC_{0-t} 662.9 \pm 8.3 \mu\text{g} / \text{L} \cdot \text{h}$ and $C_{\text{max}} 486.9 \pm 8.5 \mu\text{g} / \text{L}$. This was indicating a significant reduction in short-term simulated weightlessness rats by intramuscular injection of promethazine absorption in the body. The tail suspension significantly decreased the V_d and Cl while increased K_e a little. T_{max} was delayed 0.08h. The apparent volume of distribution V_d were elevated 12.95 times and 3.97 times separately than that of normal group's $28.0 \pm 0.04 \text{ L} / \text{kg}$. And the clearance rate Cl were extended to 8.57 times and 3.36 times of the control group $3.6 \pm 0.3 \text{ l/h/kg}$, indicating that the clearance rate was slowed down after intramuscular injection of promethazine after short-term simulated weightlessness cycles. The parameters of rats tail-suspended for 21 days were not shown clear pharmacokinetic trend.