Pharmacokinetics of higenamine in rabbits.

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Abstract

The pharmacokinetics of higenamine were investigated in rabbits by IV bolus, PO route, and IV infusion. Plasma higenamine concentration declined rapidly in a biexponential pattern, with a terminal half-life of 22 min. The AUC increased proportionally with increasing dose, whereas the percentage of unchanged higenamine excreted from urine remained constant when dose was increased. The means of total body clearance, mean residence time, volume of distribution at steady state, and fraction of urinary excretion were 127.7 mL min-1 kg-1, 9.28 min, 1.44 kg-1, and 5.48%, respectively. The mean percentage of protein binding of higenamine in plasma was 54.8% at steady state after IV infusion. The results from post-infusion also confirmed that higenamine followed a two-compartment open model in animals. After oral administration, higenamine was rapidly absorbed to reach peak concentration within 10 min. Interestingly, the plasma concentration-time profiles revealed two distinguishable groups with different Cmax, extent of absorption, and urinary excretion. The average absolute bioavailabilities of higenamine calculated by AUCs and accumulated urinary excretion were 21.86 and 2.84% versus 20.19 and 5.50% for the two groups, respectively. Upon hydrolysis of urine samples with beta-glucuronidase, urinary concentrations of higenamine were greatly enhanced in both groups.