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Study on in vivo activities of CYP3A enzyme in Bactrian camel with specific probe drug

The aim of the research is to study the in vivo activities of Bactrian camels' CYP3A enzymes by investigating the pharmacokinetic characteristics of CYP3A specific probe drug Midazolam in Bactrian camel, and the effect of Itraconazole on the pharmacokinetic behavior of Midazolam was studied simultaneously. Firstly, five healthy adult Bactrian camels were intramuscularly injected with the single dose of 0.1 mg/kg Midazolam, and then blood samples were collected from the jugular vein at different time following the administration. Secondly, after 7 days drug clearance period, these five experimental camels were injected intramuscularly with the single dose of 0.1 mg/kg Itraconazole for 4 consecutive days, and following 2 h of last injection, Bactrian camels were administered intramuscularly with the single dose of 0.1 mg/kg Midazolam again. Blood samples were collected by same route and same intervals as previous, and the plasma was separated by centrifugation. The plasma concentration of Midazolam was determined high performance liquid chromatography-UV detection, and the pharmacokinetic parameters of Midazolam were analyzed by WinNonLin 7.0 with non-compartmental model. The pharmacokinetic parameters of Midazolam in group probe drug only and in group enzyme inhibitor plus probe drug were as follows: the $T_{_{1/2}}$ was 2.5±0.073 h and 3.674±0.29 h, $T_{_{max}}$ was 0.85±0.09 h and 0.54±0.06 h, $C_{_{max}}$ was 0.62±0.12 µg/mL and 0.80±0.06 μg/mL, AUC_{0-t} was 1.47±0.35 h•μg/mL and 2.15±0.15 h•μg/mL, V_d was 259.17±41.29 mL/kg and 152.09±22.49 mL/ kg, CL was 53.46 ± 14.25 mL/h/kg and 34.3 ± 5.13 mL/h/kg, and MRT was 3.71 ± 0.16 h and 4.60 ± 0.52 h, respectively. Therefore, all the second state of the second st the $T_{1/2}$, T_{max} , C_{max} and MRT of Midazolam in Bactrian camels were relatively low which indicated that Bactrian camels' CYP3A enzyme possess high activity on metabolism of Midazolam. Furthermore, the CYP3A enzyme was significantly inhibited by Itraconazole which can increase the $T_{1/2}$, C_{max} , AUC and MRT, and can reduce the T_{max} of Midazolam in Bactrian camel.

Biography

Surong Hasi is currently working as a professor in college of veterinary medicine, inner mongolia agricultural university, and is a director of camel protection association of Inner Mongolia. His research interests are mainly focused on the pharmacokinetic characteristics of veterinary drugs in different species, drug-drug interactions in animals, pharmacological activities of camel milk and Bactrian camel CYP enzymes.

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