

## **Ketoprofen in the Cat: Pharmacodynamics and Chiral Pharmacokinetics**

### **ABSTRACT**

The non-steroidal anti-inflammatory drug ketoprofen (KTP) was administered as the racemate to cats intravenously (IV) and orally at clinically recommended dose rates of 2 and 1 mg/kg, respectively, to establish its chiral pharmacokinetic and pharmacodynamic properties. After IV dosing, clearance was more than five times greater and elimination half-life and mean residence time were approximately three times shorter for R(-) KTP than for S(+) KTP. Absorption of both S(+) and R(-) enantiomers was rapid after oral dosing and enantioselective pharmacokinetics was demonstrated by the predominance of S(+) KTP, as indicated by plasma AUC of 20.25 (S(+))KTP and 4.09 (R(-))KTP  $\mu\text{g h/mL}$  after IV and 6.36 (S(+))KTP and 1.83 (R(-))KTP  $\mu\text{g h/mL}$  after oral dosing. Bioavailability after oral dosing was virtually complete. Reduction in ex vivo serum thromboxane (TX)B<sub>2</sub> concentrations indicated marked inhibition of platelet cyclo-oxygenase (COX)-1 for 24 h after both oral and IV dosing and inhibition was statistically significant for 72 h after IV dosing. Both oral and IV rac-KTP failed to affect wheal volume produced by intradermal injection of the mild irritant carrageenan but wheal skin temperature was significantly inhibited by IV rac-KTP at some recording times. Possible reasons for the disparity between marked COX-1 inhibition and the limited effect on the cardinal signs of inflammation are considered. In a second experiment, the separate enantiomers of KTP were administered IV, each at the dose rate of 1 mg/kg. S(+))KTP again predominated in plasma and there was unidirectional chiral inversion of R(-) to S(+))KTP. Administration of both enantiomers again produced marked and prolonged inhibition of platelet COX-1 and, in the case of R(-))KTP, this was probably attributable to S(+))KTP formed by chiral inversion.

**Keyword:** Ketoprofen, cat, pharmacodynamics, pharmacokinetics, enantiomers, chirality