

PHARMACOKINETICS OF TRAMADOL AND O-DESMETHYLTRAMADOL METABOLITE IN BOA (*Boa constrictor constrictor*)

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Tramadol is commonly used for pain management, but its pharmacokinetics in reptiles, especially snakes, are not well understood. *Boa constrictors* are an ideal model for studying tramadol's absorption, metabolism, and elimination due to their unique physiological characteristics.

Ten healthy male *Boa constrictors* (4.33 ± 1.5 kg) were administered tramadol ($5 \text{ mg}\cdot\text{kg}^{-1}$) via intramuscular in the epaxial musculature at the cranial third (TRIM) or intravenous in the paravertebral vein at the cranial third (TRIV), with a 45-day interval between treatments. Blood samples were collected at various time points: 0 (before tramadol injection), 1 (20 min after injection), 2 (40 min after injection), and 3, 4, 5, 6, 7, 8, and 9 hours (1, 2, 4, 8, 12, 18, and 26 hours post-injection). The total blood collected per animal did not exceed 1% of its weight, pharmacokinetics were analyzed using high-performance liquid chromatography and a pharmacokinetic model (R software 4.3.0). A paired Student's T-test was used for all parametric variables, except clearance analyzed with the Wilcoxon test, with statistical significance set at 5%.

For the TRIM group, tramadol reached a maximum concentration of $2.58 \mu\text{g}\cdot\text{mL}^{-1}$, with a volume of distribution (V_d) of $10.58 \pm 2.91 \text{ L}\cdot\text{kg}^{-1}$, clearance of $0.36 \pm 0.07 \text{ L}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$, and a half-life of 19.96 ± 8.34 h. For the TRIV group, values were $3.39 \mu\text{g}\cdot\text{mL}^{-1}$, $5.60 \pm 1.69 \text{ L}\cdot\text{kg}^{-1}$, $0.22 \pm 0.05 \text{ L}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$, and 17.32 ± 7.55 h, respectively. The active metabolite M1 had a maximum concentration of $0.58 \mu\text{g}\cdot\text{mL}^{-1}$ (TRIM) and $0.59 \mu\text{g}\cdot\text{mL}^{-1}$ (TRIV), with half-lives of 49.89 ± 10.8 h and 35.66 ± 10.85 h. Tramadol's intramuscular bioavailability was 61%, with M1 detectable 20 minutes after administration.

Tramadol is rapidly converted into M1, maintaining high concentrations for extended periods. The intramuscular route proves to be a viable alternative due to its favorable bioavailability in *Boa constrictors*.