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## PHARMACOKINETICS OF A SINGLE DOSE OF METRONIDAZOLE IN CAPTIVE ASIAN ELEPHANTS (*Elephas maximus*)

Samantha Sander, DVM,<sup>1\*</sup> Jessica Siegal-Willott, DVM, Dipl ACZM,<sup>1</sup> Elizabeth Lee,<sup>2</sup> Lisa Tell, DVM, Dipl ABVP, Dipl ACZM,<sup>2</sup> Jessie Ziegler, DVM, MS,<sup>3</sup> and Suzan Murray DVM, Dipl ACZM<sup>4</sup>

<sup>1</sup>Wildlife Health Sciences, National Zoological Park, Washington DC 20013 USA;

<sup>2</sup>Department of Medicine and Epidemiology, School of Veterinary Medicine, University of California-Davis, Davis, CA 95616 USA; <sup>3</sup>Ringling Brothers Center for Elephant Conservation, Polk City, FL 33868 USA; <sup>4</sup>Smithsonian Conservation Biology Institute, National Zoological Park, Washington, DC 20013 USA

### Abstract

Metronidazole is a nitroimidazole drug with bacteriocidal activity against a broad range of anaerobic bacteria.<sup>1,3</sup> It is a recognized treatment for elephants exhibiting signs of colonic impaction, diarrhea, colic, protozoal disease, or anaerobic bacterial infection.<sup>1</sup> The purpose of this study was to evaluate the pharmacokinetics of rectally administered metronidazole<sup>a</sup> (15 mg/kg) in adult female Asian elephants (*Elephas maximus*, n = 6). Serum samples were collected from each animal at the following times: 0, 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 8, 12, 16, 24, 36, 48, 60, 72, 84 and 96 hr post rectal administration of metronidazole. Serum concentrations of metronidazole and its primary metabolite hydroxymetronidazole were measured via ultra performance liquid chromatography. Data were analyzed via a noncompartmental pharmacokinetic approach. Results indicated that serum levels of metronidazole were quantifiable at 0.25 hr and absent by the 96-hr time point in all elephants. The serum peak concentration (mean  $\pm$  SD 13.15  $\pm$  2.59  $\mu$ g/ml) and mean area under the curve from time 0 to infinity (mean  $\pm$  SD was 108.79  $\pm$  24.77 hr \*  $\mu$ g/ml) were higher than that reported in horses after rectal administration of metronidazole at similar doses.<sup>2,4</sup> Concurrently, the time of maximum serum concentration (mean  $\pm$  SD 1.2  $\pm$  0.45 hr) and terminal elimination half life (harmonic mean  $\pm$  pseudo-SD 7.85  $\pm$  0.93 hr) were longer when compared to equine reports.<sup>2,4</sup> Rectal administration of metronidazole was well tolerated and rapidly absorbed in Asian elephants. Dosing recommendations will depend on the mean inhibitory concentration of metronidazole for each pathogen.

<sup>a</sup>Metronidazole, Watson Pharma, Parsippany, NJ 07054 USA.

**Key words:** Asian elephant, *Elephas maximus*, Metronidazole, pharmacokinetic, rectal

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