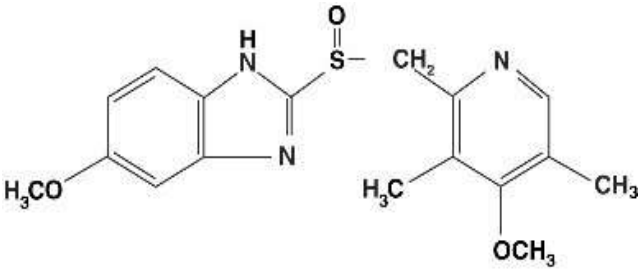
CONTROLLED THERAPEUTIC MEDICATIONS

MONOGRAPH SERIES

Omeprazole

Background



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Omeprazole is an anti-ulcer medication commonly used in performance horses in the treatment and prevention gastric and duodenal ulcers and equine gastric ulcer syndrome (EGUS) and as a component of pre-surgical protocols when withholding of feed is required.[i] It is assigned 5/D in the ARCI's Uniform Classification of Foreign Substances. Omeprazole is a protein pump inhibitor that inhibits gastric acid production. Omeprazole differs from other ulcer medications because it blocks gastric acid secretion through irreversible inhibition of hydrogen- potassium adenosine triphosphatase (protein pump). This irreversible binding prolongs the anti-secretory effects and allows for once daily administration.[ii]

Omeprazole is available over the counter for human use in tablet and capsule formulations such as Prilosec™ or Nexium™ and for equine use as the paste Ulcer Gard™. Omeprazole, in some formulations, such as GastroGard™, is a prescription medication and may only be dispensed or administered on the order of a veterinarian.[iii] It is most commonly administered as a paste that protects the drug from degradation from the stomach's acidic pH.[iv] Omeprazole decreases acid production in a dose dependent manner. The manufacturer-recommended dose is 4 mg/kg, PO, every 24 hours for 4 weeks followed by a 2 mg/kg, PO, dose every 24 hours for at least another 4 weeks to prevent ulcer recurrence. Compound formulations of omeprazole have been found less effective in ulcer treatment than proprietary formulations.[v]

Ulcers affect between 58-100% of adult horses in training. Meaning most racehorses will develop gastric ulceration at some time in their careers, although not all affected horses show clinical signs. [vi] Gastric ulcers in performance horses has been correlated with poor coat, selective eating, signs of abdominal discomfort, and decreased performance.[vii] Omeprazole can be administered long-term and as an ulcer prevention method long term with no adverse effects.[viii] Omeprazole has become the "gold standard" of antiulcer treatment in horses due to its easy administration and its ability to significantly decrease ulceration in as little as 7 to 14 days.[ix]

Administration Study

Omeprazole was administered in the form of Gastrogard® oral paste at a dose of 2.28 g per horse (3.7-5.2 mg/kg) once daily for a total of four doses to nine healthy exercise-conditioned adult Thoroughbred horses at Kentucky Equine Research (Versailles, KY).[x] This dose selection was determined based on an informal survey of equine practitioners conducted by the Racing Medication and Testing Consortium. The horses were fed one hour after drug administration.

Blood Samples were obtained immediately before administration and at 1, 2, 4, 6, 12, and 24 hours after the first dose. Samples were collected at 1, 2, 4, 6, 12, 24, 36, 48 hours after the last administration. Additional samples were collected at 12-hour intervals during the administration period.

Extraction and Analysis Procedure

Quantification of omeprazole in plasma was performed at the School of Veterinary Medicine, University of California, Davis using validated methods. Omeprazole was determined in plasma concentrations by liquid chromatography-mass spectrometry (LC-MS/MS) using a refence standard obtained from Cerilliant Corporation (Round Rock, TX) to verify accuracy and precision. The Limit of Quantification (LOQ) for determination of omeprazole in plasma was 0.1 ng/mL and the Limit of Detection (LOD) was 0.03 ng/mL.

Pharmacokinetic Modeling

Plasma concentrations of omeprazole are expressed as the median and range at each collection point (Table 1.1). Pharmacokinetic analysis was performed on individual plasma concentrations using Pheonix® WinNonlin® pharmacokinetic analysis software (Pharsight Corporation, Cary, NC).

Results and Discussions

Concentrations varied widely between horses at each time point but were below LOQ in all horses upon termination of sample collection. The terminal elimination half-life for omeprazole ranged from 3.02 to 6.33 hours. Mean, median, and range of the omeprazole sulfide plasma concentrations at select time points after administration are shown in Table 1.1 below.

Table 1.1 Mean ± SD and range of serum omeprazole sulfide concentrations following 2.28 g SID (4 doses) at 24 hours following the final oral administration to nine exercised Thoroughbred horses.

Time (hours)	Mean ± SD (ng/mL)	Median (ng/mL)	Range (ng/mL)
24	0.33 ± 0.46	0.20	0.02-1.50

Scientific Advisory Committee (SAC) Recommendation

The 95/95 Tolerance Interval calculation was applied to the data at the 24-hour collection time point. The resultant value of 6.96 ng/mL was rounded up by the SAC to a recommended threshold of 10 ng/mL of omeprazole sulfide in serum/plasma corresponding to 24-hour withdrawal based in an oral administration of 2.2 grams once daily for 4 days.

Practice Tips

Some regulatory authorities have a prohibition on the administration of medication within 48 hours of a race. RMTC recommendations do not supersede rules or regulations. Veterinarians and horsemen are responsible for knowing and complying with regulations in the jurisdictions in which they train and race.

Horsemen may elect to administer once daily dosing of omeprazole in conjunction with afternoon feedings. This will allow for uninterrupted daily treatments, as omeprazole can be administered at 24 hours prior to racing and then after racing.

Different formulations of omeprazole, use of compounded products, administration of higher doses, use of other administration methods, or combinations of omeprazole with other substances represent unknown risk for a concentration in excess of the threshold and therefore an extended withdrawal time is recommended. Veterinarians are advised to use caution when deviating from doses and routes that have been studied and to use an extended withdrawal time and/or submit a sample for analysis prior to competition.

References

[i] Knych, H.K. *et al*, *Disposition of the Anti-ulcer Medications Ranitidine, Cimetidine, and Omeprazole Following Administration of Multiple Doses to Exercised Thoroughbred Horses,* J. Vet. Pharmacol. Therap. 2017 Jan 40(1):92-6.

[ii] Bell, R.J.W. *et al*, *Equine Gastric Ulcer Syndrome in Adult Horses: A Review*, New Zealand Vet. J., 2007, 55(1): 1-12.

[iii] FDA Green Book. https://animaldrugsatfda.fda.gov/adafda/views/#/search (Enter omeprazole in the search box)

[iv] Nieto, J.E. *et al*, Effect of Gastric Ulceration on Physiologic Responses to Exercise in Horses, AJVR, 2009, 70(6): 787-795.

[v] Orsini, J. A. *et al*, *Odds of Moderate or Severe Gastric Ulceration in Racehorses Receiving Antiulcer Medications,* JAVMA, 2003, 223(3): 336-339.

[vi] Bell, RJW *et al*, New Zealand Vet. J., 2007.

[vii] Nieto, J.E., *et al.,* AJVR, 2009.

[viii] McClure, S.R. *et al*, *Efficacy of Omeprazole Paste for Prevention of Gastric Ulcers in Horses in Race Training*, JAVMA, 2005, 226(10): 1681-1684.

[ix] Orsini, J.A., *et al.,* JAVMA, 2003.

[x] Knych, H.K. *et al.,* J. Vet. Pharmacol. Therap., 2017.