Boehringer Ingelheim

Pharmacokinetics Comparisons

Technical Bulletin

Boehringer Ingelheim Vetmedica, Inc.

Key Points

BIO-MYCIN® 200 and Tetradure™ 300

- Despite the increased dose of Tetradure™ 300, the pharmacokinetic parameters were not significantly different from **BIO-MYCIN® 200** for most parameters.
- Tetradure™ 300 total Area Under the Curve (AUC) was significantly greater than **BIO-MYCIN 200** but not 1.5 times the value of **BIO-MYCIN 200**.

Study Design

Investigators	Patricia M. Dowling, DVM, MVS, DACVIM, DACVCP, Western College of Veterinary Medicine, Saskatoon, Saskatchewan Chris Clark, VetMB, MVSc, Western College of Veterinary Medicine
Study animals	Six yearling mixed breed heifers Calves received no oxytetracycline medication during previous 30 days Calves weighted from 836 to 1034 lb
Procedure	Double-blinded cross-over design Calves randomly assigned to two groups of three calves Each calf received the assigned treatment Group 1: Received **BIO-MYCIN 200** at 20 mg/kg Sub-Q* Group 2: Received Tetradure™ 300 at 30 mg/kg IM* Data collected After a two week wash out period, each group received the opposite product Group 1: Received Tetradure™ 300 at 30 mg/kg IM* Group 2: Received **BIO-MYCIN 200** at 20 mg/kg Sub-Q*
Date	October 2001

*No more than 10 mL was given per injection site; both were administered as recommended by product manufacturer.

Data Collection

Blood samples were collected prior to drug administration and at 15, 30, and 45 minutes after treatment.

Sampling continued at 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 12, 24, 36, 48, 60, 72, 84 and 96 hours after treatment.

Plasma samples were assayed by high performance liquid chromatography.

Due to insufficient plasma at several time points, one calf was excluded of the entire study. With cross-over design and low variability of the data this deletion did not affect statistical power for calculations.

All pharmacokinetic parameters were compared using a one sample T-test.

www.productionvalues.com
2621 North Belt Highway
St. Joseph, MO 64506-2002

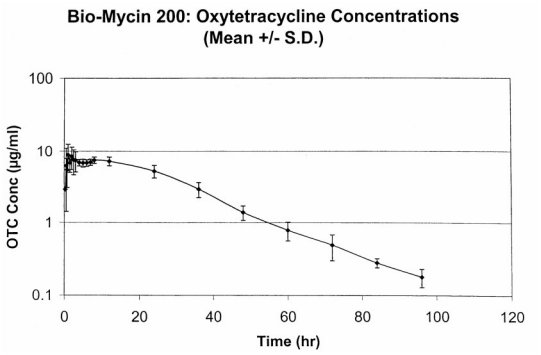
Parameters Measured

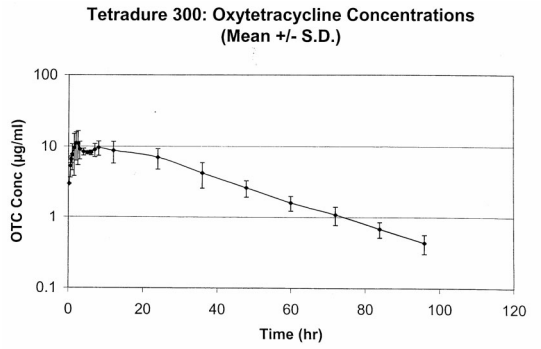
- Drug plasma concentration versus time plotted as Area Under the Curve (AUC) and AUC for 48 hours (AUC-48)
- Elimination half-life ($T^1/_2$) of the drug
- Maximum oxytetracycline concentration (C_{max})
- Time to reach C_{max} (T_{max})

Results

All pharmacokinetic parameters were compared using a one sample T-test on the difference between the parameters. Only AUC was significantly ($p<0.05$) different between the two antibiotics.

	Bio-Mycin® 200	**Tetradure™ 300**	
Parameter	**Mean & (Standard Deviation)**	**Mean & (Standard Deviation)**	**Statistical Difference Level**
C_{max} (microgram/mL)	8.92(1.89)	10.72 (1.44)	No difference
T_{max} (hours)	3.3 (1.9)	4.7 (2.0)	No difference
AUC (microgram/mL/hr)	249 (28.4)	384 (68.9)	P<0.05
AUC-48 (microgram/mL/hr)	234 (23.9)	309 (85.3)	No difference
Half life $T^1/_2$ (hours)	17.5	20.8	No difference





Clinical Significance

These investigators indicate that in the treatment of bacterial infections in cattle, oxytetracycline is considered a time-dependent antimicrobial. Clinical efficacy correlates with the time the drug concentrations remain above the bacterial minimum inhibitory concentration (MIC). MIC varies widely for the many bacteria potentially treated with oxytetracycline. The therapeutic efficacy of oxytetracycline in cattle is usually associated with maintaining plasma concentrations above 0.5 micrograms/mL during the dosage interval.

At a dose of 20 mg/kg, **Bio-Mycin 200** plasma concentrations dropped below 0.5 micrograms/mL at 72 hours. Tetradure 300 concentrations dropped below this level at approximately 90 hours. Based on the results of this study, using Tetradure 300 at 1.5 times the dosage of **Bio-Mycin 200** did result in increased plasma oxytetracycline consistent with the increased dose, but not equal to 1.5 times **Bio-Mycin 200** AUC levels. There was no statistical difference between the treatments AUC for the first 48 hours post-dosing or in the maximum plasma concentration attained. The investigators indicated most of the difference between the two treatments occurred in the prolonged low plasma concentrations of the Tetradure 300 formulation at the end of the plasma concentration time curve.

The Bottom Line

- **Bio-Mycin 200** at 20 mg/kg resulted in plasma concentrations of oxytetracycline with no significant difference to Tetradure 300 at 30 mg/kg for: AUC-48, C_{max}, $T_{max,}$ and $T^1/_2$.
- Tetradure 300 did show significantly greater total amount of oxytetracycline delivered to the plasma for the total time measured (AUC); it was not 1.5 times the level of **Bio-Mycin 200** plasma levels.