

Plasma and Lung Tissue Levels of Aureomycin® and Oxytetracycline in Calves at Various Time Periods After Oral Administration at 10 mg/lb Body Weight for Five Days

Introduction

Aureomycin (chlortetracycline) is a member of the tetracycline class of antibiotics. While members of this class are similar in molecular structure, there are pharmacological differences between tetracyclines that must be considered when utilizing them for disease management. It has been demonstrated that Aureomycin may have a greater affinity for lung tissues than oxytetracycline (OTC)¹, which suggests that it is the preferred product for use in managing bovine respiratory disease. Concentrations of a medication in tissue may in part be dependent on lipid solubility. Those medications with greater lipid solubility should move across cell membranes more freely, and, thus, become more available for antimicrobial activity. Examination of two different partition coefficients for chlortetracycline and oxytetracycline show that chlortetracycline is more lipid soluble between pH 2 to 8.^{2,3}

A study was conducted to identify differences in antibiotic concentrations that might exist in plasma and lung tissue when Aureomycin or OTC were administered to ruminating calves at 10 mg/lb BW for 5 days.

Materials and Methods

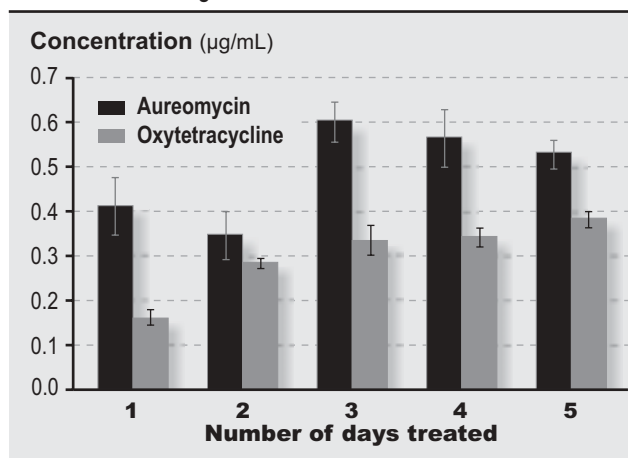
A high performance liquid chromatography (HPLC) method of assaying bovine plasma and lung tissue was developed and validated by Health of Animals Laboratory, Saskatoon, Saskatchewan, Canada. The limit of quantitation for Aureomycin and OTC, respectively, in plasma and tissue was 0.100 and 0.050 µg/mL or µg/g.

Aureomycin 50G Type A medicated premix and Terramycin 50 g/lb medicated premix were the test articles. Each premix was assayed prior to start of the study, and dosages administered were based on actual assay values.

Fifty-one ruminating Holstein calves were utilized to determine Aureomycin and OTC levels in plasma and lung tissue. One calf was removed from the study due to illness. A replacement animal was utilized. Prior to initiation of the study, plasma from all calves were determined to be devoid of Aureomycin or OTC. Calves were allotted by weight to treatment groups so that individual weights within groups and total weights of treatment groups were similar. Weights of calves used in the blood and lung tissue portion of the study ranged from 101 to 440 pounds with a mean weight of 309 pounds.

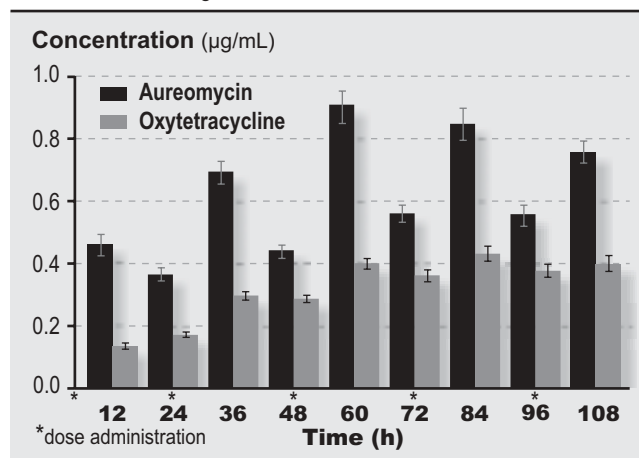
All calves were maintained on an alfalfa hay diet for the duration of the study. Calves in each treatment group were administered either Aureomycin or OTC at a dosage of 10 mg/lb body weight via gelatin capsule once daily for 5 days. Following administration, blood samples were

FIGURE 1: Plasma Aureomycin and OTC concentrations (± standard error) after 1 to 5 days administration at 10 mg/lb BW.



n = 5 per treatment; all values are 24 hours post final dose.

FIGURE 2: Plasma Aureomycin and OTC concentrations (\pm standard error) after 1 to 5 days administration at 10 mg/lb BW.



0 hr: n=31, all treatments decreased by 5 hd each 24 hours.
96 h: n=25 Aureomycin and 31 OTC decreased by 5 hd each 24 h.
Plasma samples were obtained prior to dose administration.

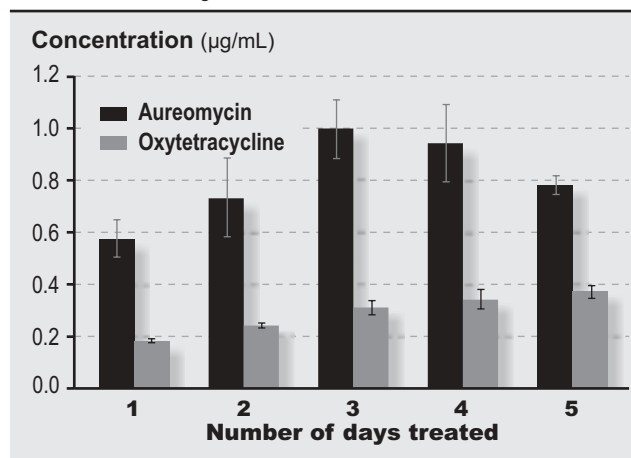
obtained 12 and 24 hours after each dose. Groups of 5 calves were euthanized with a captive bolt 24 hours after day 1, 2, 3, 4 and 5 of Aureomycin and OTC administration. Lung tissue samples were obtained from each euthanized calf at 24, 48, 72, 96 and 120 hours after the start of treatment. The original experimental design was expanded by adding 9 Aureomycin and 15 OTC calves to the depletion portion of the study. Blood samples were collected from those calves starting at hour 96.

Additional groups of 5 calves from each treatment group were euthanized at 24, 48, 72 and 96 hours after 5 days of drug administration to determine “tetracycline” antibiotic depletion rates and durations. A group of 5 OTC calves were euthanized after 120 hours (5 days) post-administration. At the time of euthanization, plasma and lung tissue samples were obtained for assay of respective tetracycline. Weights of calves used in the drug depletion portion of the study ranged from 219 to 445 pounds with a mean weight of 333 pounds after assignment to groups.

Results

Plasma levels of Aureomycin peaked at day 3, while concentrations for Terramycin increased through day 5. Except for day 2, Aureomycin attained higher levels ($P < 0.05$) in plasma on all days (Figure 1). At 108 hours post-administration, Aureomycin was detected at greater ($P < 0.05$) concentrations than oxytetracycline (Figure 2).

FIGURE 3: Lung Aureomycin and OTC concentrations (\pm standard error) after 1 to 5 days administration at 10 mg/lb BW.

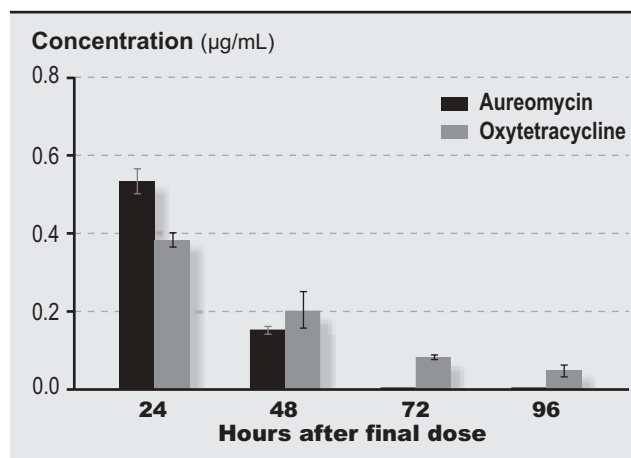


n = 5 per treatment per day; all values are 24 hours post final dose.

Likewise, lung tissue levels for Aureomycin increased until day 3 and then declined, whereas concentrations for OTC increased through day 5. On all days, however, Aureomycin achieved higher levels ($P < 0.05$) in the lung tissue than OTC (Figure 3).

Aureomycin was detected in plasma in greater concentrations ($P < 0.05$) than OTC when measured 24 hours after 5 successive days of administration. Forty-eight hours

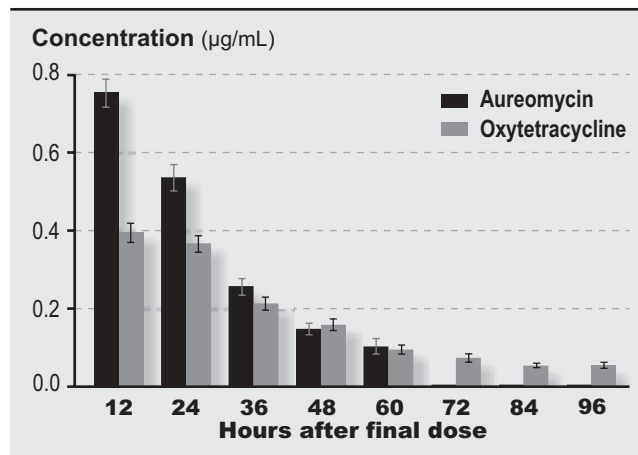
FIGURE 4: Aureomycin* and OTC plasma concentrations (\pm standard error) 24 to 96 hours post-administration.



n = 5, both treatments; animals dosed 5 days.

*non-detectable at limits of quantitation at 48 hours post-administration.

FIGURE 5: Mean plasma Aureomycin and OTC concentrations (\pm standard error) after 5 consecutive days administration.



n = 5

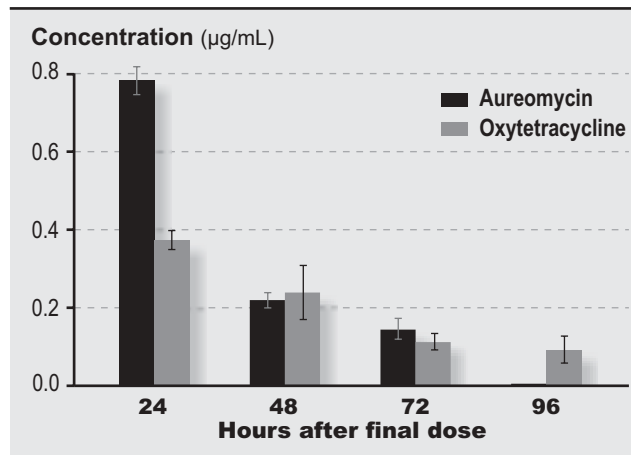
post-administration, Aureomycin was present at a lower ($P < 0.05$) concentration than OTC, and 72 and 96 hours post-administration Aureomycin was undetectable. OTC remained detectable after 72 and 96 hours of drug withdrawal (Figure 4). Extended depletion assays revealed greater ($P < 0.05$) concentrations of Aureomycin than OTC at 12 and 24 hours post-administration, but no differences were detected at 36, 48 and 60 hours. OTC remained detectable 72, 84, and 96 hours after drug withdrawal, while Aureomycin was not (Figure 5).

Lung tissue concentrations of Aureomycin were greater ($P < 0.05$) 24 hours post-withdrawal than were those of OTC. At 48 and 72 hours, Aureomycin and OTC were similar. At 96 hours, OTC remained detectable, whereas Aureomycin was not detectable (Figure 6).

Conclusions

Aureomycin dosed at 10 mg/lb BW reached higher concentrations in both plasma and lung tissue of ruminating calves than did OTC. Aureomycin was eliminated from plasma and lung tissue at a faster rate than was OTC. When the decision is made to treat cattle for bovine respiratory disease through the feed with a "tetracycline," the results of this study indicate that Aureomycin should be the "tetracycline" of choice.

FIGURE 6: Aureomycin and OTC lung concentrations (\pm standard error) after 5 days administration at 10 mg/lb BW.



n = 5, both treatments; animals dosed 5 days.

Literature Cited

1. Antimicrobial Blood and Lung Tissue Levels in Cattle Fed Aureo S 700 or Oxytetracycline (Alpharma Technical Bulletin CD 0330).
2. Aronson. Pharmacotherapeutics of the newer tetracyclines. *JAVMA* 1980; 176 (10 Spec No): 1061-1068.
3. Colaizzi et al. pH-Partition behavior of tetracyclines. *J Pharm Sci* 1969; 58:1184-1189.