

# Effect of topical treatment of claw horn lesions with tetracycline-derivatives on plasma and milk concentrations

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## Introduction:

Claw horn lesions frequently result in lameness, and these types of lesions are associated with environment and animal husbandry practices rather than infectious pathogens. The paucity of scientific literature pertaining to intervention strategies for these lesions promote therapeutic trimming techniques with or without the application of a hoof block to the contralateral claw and producer-dependent use of systemic antibiotics and analgesics. In a recent survey of hoof trimmers and veterinarians, 53% of trimmers and 59% of veterinarians reported using topical application of medications to solar lesion, with extra-label use of tetracycline-derivatives being the most frequently reported topical medication. In the advent of modern analytical technology, more sensitive assays are available to detect pharmaceuticals present in consumable animal products. These assays offer a more sensitive evaluation of residues involving the topical application of tetracycline-derivatives, which warrants concerns over the potential for violative residues. Given these lesions result in exposure of raw corium and granulation tissue, the potential of topical medications entering the systemic blood circulation in treated animals is possible, and yet, no research has assessed if extra-label use of tetracycline-derivatives results in violative drug residues in plasma and milk. Our hypothesis is extra-label use of tetracycline-derivatives results in drug residues in both plasma and milk; however, the concentrations would not surpass the Food and Drug Administration's reported acceptable level, 300 ppb.

## Materials and Methods:

Eight Holsteins and 3 Jerseys diagnosed with either a sole ulcer or a white line lesion at hoof trimming events were topically treated with either oxytetracycline HCl (7 animals) or tetracycline (4 animals). Digital images were taken of each lesion. The 7 animals treated with topical oxytetracycline HCl received 7.3 grams of active ingredient. Prior to treatment, milk and plasma samples were collected. Following treatment, plasma was collected once a day for 3 days, and milk was collected at each milking (3 times per day) for 3 days. The 4 animals topically treated with tetracycline had milk and plasma samples collected prior to treatment. Following treatment, milk and plasma samples were collected twice a day for 3 days. Plasma and milk samples were frozen after collection and submitted to Iowa State's Pharmacology Analytical Support Team

(PhAST) laboratory where drug concentrations were quantified using liquid chromatography-mass spectrometry. To calculate lesion surface area, the digital images were evaluated using free software, ImageJ, available through U. S. National Institute of Health. Statistical analysis was performed using JMP (JMP 10.00, SAS Institute, Cary, NC).

## Results:

The C<sub>max</sub> for tetracycline in plasma (mean ± SEM, 4.78 ± 2.82 ng/ml; 95% confidence interval [CI], -4.40 to 13.95 ng/ml) was recorded at the time the medicated bandage was applied, and the C<sub>max</sub> for tetracycline in milk (mean ± SEM, 20.64 ± 14.51 ng/ml; 95% CI, -12.17 to 53.46 ng/ml) was recorded at the 3<sup>rd</sup> milking (milking 2x/day). The C<sub>max</sub> for oxytetracycline in plasma (mean ± SEM, 2.15 ± 1.20 ng/ml; 95% CI, -0.52 to 4.81 ng/ml) was recorded at 48 hours post topical application, and the C<sub>max</sub> for oxytetracycline in milk (mean ± SEM, 20.81 ± 19.90 ng/ml; 95% CI, -27.88 to 69.51 ng/ml) was recorded at the 7<sup>th</sup> milking (milking 3x/day). Greater log-transformed surface area measurements of lesions tended to be positively associated with higher log-transformed drug concentrations in both plasma ( $R^2=0.51$ ;  $P=0.03$ ) and milk ( $R^2=0.44$ ;  $P=0.03$ ).

## Significance:

Results suggested cows with larger claw lesions exposed to tetracycline derivatives tend to absorb more drug into systemic circulation. Tetracycline concentrations are inclined to peak faster in both plasma and milk when compared to oxytetracycline HCl. It was noted that the time zero concentration for the 3 of the 4 tetracycline plasma samples contained a trace of drug, and due to the levels being so low, we hypothesize this is contamination from the trimmer's hands at the time of plasma collection. Plasma drug levels were lower than milk concentrations likely because the sampling schedule was designed to capture drug depletion in milk as opposed to the systemic circulation. Milk concentrations therefore represented the cumulative secretion of drug in the milk between milkings. Although it is shown that tetracycline-derived residues do enter systemic circulation and ultimately milk following topical application of medicated hoof wraps, the level of drug reported is unlikely to result in residue violations if administered to individual cows.