Utilization of Liquid Chromatography/Mass Spectrometry to Detect Drug Residues in Milk: Applications for Research and Commercial Dairying

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Introduction

Prevention of drug residues in milk is a daily endeavor on dairy farms. There is increasing scrutiny from the public and government when it comes to drug residues in milk. Drug residues can result from simple human errors, disease processes not allowing for normal clearance of a drug, or malicious activity. The testing methodologies used to detect drug residues have become more sensitive with many tests available that can detect drug levels below ten parts per billion (ppb).

There is a vast amount of drug pharmacological information published about the clearance of drugs from dairy cattle but most is limited to clearance of drugs in healthy animals and tissues. One such example is the use of oxytetracycline infusions to treat metritis in dairy cattle. While the clinical effectiveness is debatable, the use of oxytetracycline for the treatment of metritis is an extremely common practice on many dairy farms. Despite its widespread use in the dairy industry, there is very little known about the pharmacology of oxytetracycline intrauterine infusions in dairy cattle.

Research conducted by ISU's College of Veterinary Medicine looked to see if there was a correlation between uterine pathology and levels of oxytetracycline in milk and plasma following intrauterine infusion. The aim of the research was to determine if: 1) oxytetracycline entered the plasma and milk after intrauterine infusion; 2) the residue level of oxytetracycline if it entered the plasma and milk and; 3) relationship between uterine pathology and oxytetracycline levels.

Materials and Methods

Thirty Holstein cows diagnosed with metritis were enrolled into this study. Upon diagnosis of metritis, the severity of the disease was quantified (mild, moderate, or severe), milk and blood samples were collected from the cow prior to treatment and then the cows received an intrauterine infusion of four grams (4 gm) oxytetracycline. Blood samples were taken daily for seven days and milk samples were collected twice daily for seven days in order to monitor the concentration of oxytetracycline in plasma & milk.

The Pharmacology Analytical Support Team (PhAST) at the ISU Veterinary Diagnostic Laboratory (VDL) performed quantification of oxytetracycline concentrations. Residues concentrations were determined by liquid chromatography-mass spectrometry (LC-MS/MS). Plasma and milk pharmacokinetic parameters were then compared with endometritis scores using a statistical screening tool.

Results

The mean maximum concentration of oxytetracycline in plasma was 0.23± 0.05 μg/mL (95% CI; 0.11 – 0.35 μg/mL). The mean maximum concentration of oxytetracycline in milk was 0.20± 0.06 μg/mL (95% CI; 0.05 – 0.35 μg/mL). The time to mean maximum concentration for plasma and milk was 24 hours and 37 hours respectively. The mean (±SEM) plasma elimination half-life of oxytetracycline after intrauterine infusion was 21.68 ± 11.16 h (95% CI; 13.1 – 30.3 h). The mean (±SEM) milk elimination half-life of oxytetracycline after intrauterine infusion was 12.03 ± 0.99 h (95% CI; 9.76 – 14.30 h). Uterine pathology scores were associated with higher area under the milk oxytetracycline and time curve (R^2 = 0.64; P= 0.0089).

Research Conclusion

This research demonstrates that oxytetracycline does enter into the plasma and milk after infusion. Uterine pathology leads to increased risk of oxytetracycline residues. These findings can aid veterinarians in establishing withdrawal time points for milk and meat after intrauterine oxytetracycline infusion.

Antibiotic Milk Residue Screen-Commercial Application

The PHAST Lab at ISU Diagnostic Lab offers a milk residue panel available that tests for up to 41 different compounds; including several classes of antibiotics, NSAID's and anthelmintics. The testing is based on liquid chromatography-mass spectrometry (LC-MS/MS). The test can detect and quantitate drug residue levels as low as 1 ppb for many of the drugs. This panel has successfully been utilized in several accidental drug exposures on dairy farms to help determine whether the milk is legal, and therefore safe, to be processed for human consumption.