We hypothesized that a novel oral suspension of potentiated sulfonamide would reach adequate tissue concentrations greater than the in vitro MIC reported for common uterine pathogens. The objective of our experiment was to assess the concentrations of sulfadiazine-trimethoprim in plasma and the endometrium in non-pregnant mares following treatment with an oral formulation.

To test our hypothesis, twenty healthy cycling mares, (ages 3 to 18 y; median 10.5 y) had endometrial biopsies performed and were declared free of endometrial inflammation per histology. In a subsequent estrus, transrectal ultrasonography was performed on the mares to determine the presence of uterine edema and a follicle ≥30 mm in diameter. These mares were treated (0 h) with a suspension of sulfadiazine-trimethoprim (333 mg/67 mg combination per mL; Equisul-SDT®, Aurora Pharmaceuticals, LLC, Northfield, MN) at a dosage of 24 mg/kg administered PO (nasogastric gavage) every 12 h for five treatments. Blood samples were obtained at 0 h, 12 h, 36 h and 60 h. An endometrial biopsy was also performed at 60 h and endometrial samples were snap-frozen in liquid nitrogen. Drug concentrations in the endometrial tissue were determined by liquid chromatography. A Pearson product-moment correlation test was used to measure the strength of association of the relative concentrations of antimicrobials in the plasma and endometrium.

Concentrations of plasma antibiotics increased with time during treatment. Mean (±SEM) concentrations of plasma sulfadiazine were 5.17±0.34, 10.22±0.64 and 13.39±0.71 µg/mL and of trimethoprim 0.038±0.01, 0.15±0.03 and 0.27±0.04 µg/mL at 12, 36 and 60 h, respectively. Endometrial concentrations of sulfadiazine and trimethoprim at 60 h were 7.96±0.47 µg/g and 0.23±0.03 µg/g, respectively. The correlation coefficients between plasma and endometrial tissue concentration of sulfadiazine and trimethoprim were R²=0.81 and R²=0.94 (p<0.0001), respectively.

Sulfadiazine-trimethoprim concentrations achieved in the endometrium after five consecutive treatments with the oral suspension were above the in vitro MIC reported for common pathogens known to cause bacterial endometritis, e.g., *Streptococcus zooepidemicus* (MIC= 0.25 to 4 µg/mL) and *Escherichia coli* (>0.25 to 4 µg/mL). The oral suspension of sulfa-trimethoprim should be an efficacious and viable treatment for bacterial endometritis.

**Keywords:** bacterial endometritis, sulfadiazine, trimethoprim, antibiotic tissue penetration, endometrium.