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Impact of MECADOX® (CARBADOX) on Pharmacokinetics of Orally Administered Oxytetracycline in Swine

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Introduction and Objective

Mecadox® is a feed additive that has been shown to control enteric disease and improve the rate, efficiency and composition of growth in swine.[1] Earlier research suggests these growth-promoting benefits of Mecadox are partly attributed to a thinner and healthier small intestine resulting in increased nutrient absorption.[2,3,4] This study used 64 growing swine in a single-dose, blood-level bioavailability study to determine if dietary carbadox affected the absorption or elimination of orally administered oxytetracycline (OTC).

Materials and Methods

Pharmacokinetic characteristics of a single oral dose of OTC (22 mg /kg of body weight by gavage) were evaluated in 16 castrate males and 16 females fed a diet containing 27.5 mg of Mecadox/kg of feed for seven days prior versus 16 animals of each gender fed a nonmedicated control diet. Blood samples were obtained via vena cava venipuncture prior to dosing with OTC and at the following times after dosing: 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 20, 24, 30, 36, and 48 hours. Serum was harvested and OTC concentration in each sample was determined by a validated microbiological cylinder plate assay. Maximum serum concentration (C_{max}, μg/mL), time at maximum concentration (T_{max}, h), area under the curve ($AUC_{0\text{-}LOQ}$, μg/mL•h), and elimination half-life ($t_{½}$, h) of OTC for each animal were calculated and statistically analyzed.

Results and Discussion

The time to maximal serum concentration (T_{max}) of 3.19 h after oral gavage, the elimination half-life ($t_{1/2}$) of 5.08 h, and the integrated area under the serum OTC concentration by time curve ($AUC_{0\text{-}LOQ}$ = 8.968 μg/mL•h) in animals fed the Mecadox diet did not differ significantly from the T_{max} (3.13 h), $t_{1/2}$ (5.12 h), and $AUC_{0\text{-}LOQ}$ (7.545 μg/mL•h) values calculated for animals fed the nonmedicated diet (Table 1). However, the maximal serum concentration (C_{max}) of OTC observed in the Mecadox fed animals was nearly 25% higher than that calculated for animals fed the nonmedicated diet (1.039 vs. 0.833 μg/mL, P=0.067). The upper and lower 90% confidence limits for T_{max} and $t_{1/2}$ of serum OTC in animals fed Mecadox readily encompass the means calculated for non-medicated animals. However, the 90% confidence interval for C_{max} of animals fed Mecadox was 2.9% to 51.1% of the mean of C_{max} for non-medicated animals.

Table 1. OTC pharmacokinetic measurements in pigs fed Mecadox and non-medicated diets

	Treatment Diet			90% Confidence Interval [a]	
Parameter	Non-med	Mecadox	P-value	Lower bound, %	Upper bound, %
T_{max} (h)	3.13[b]	3.19	0.901	-27.8	31.8
C_{max} (μg/mL)	0.833	1.039			
ln C_{max}	- 0.183	0.038	0.067	2.9	51.1
$AUC_{0\text{-}LOQ}$ (μg/mL•h)	7.545	8.986			
ln AUC	2.021	2.196	0.134	-2.1	44.9
$T_{1/2}$ (h)	5.12[b]	5.08	0.856	-7.1	5.9

[a] The upper and lower bounds of the 90% confidence interval of the variable for the animals fed Mecadox expressed as a percentage difference from the variable calculated for animals fed the non-medicated diet

[b] Means are arithmetic means for T_{max} and $T_{1/2}$. All others are geometric means

These confidence intervals demonstrate that Mecadox did not interfere with the absorption of OTC, but instead suggest that the bioavailability of OTC tended to be enhanced by dietary carbadox. To further examine this possibility, the geometric mean serum OTC concentrations through 12 hours after dosing were fitted to an equation representing a single-compartment pharmacokinetic model with oral drug administration. The OTC absorption rate constant for animals fed Mecadox was estimated to have a 95% asymptotic confidence interval of 0.619 to 0.773 h^{-1} which exceeded that calculated for animals fed the nonmedicated diet (0.477 to 0.596 h^{-1}). These results support the interpretation that dietary carbadox increased the bioavailability of oxytetracycline by enhancing its rate of absorption from the gastrointestinal tract.

Mecadox is a registered trademark of Phibro Animal Health for carbadox

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