

Tiamulin (Denagard®) by injection – PK/PD relationships with *M. hyorhinis* and *M. hyopneumoniae*

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Introduction

Tiamulin by injection (Denagard® - Novartis AH Inc.) was shown to be particularly effective against *Mycoplasma hyorhinis* (MHR) associated arthritis in young growing swine, causing a marked reduction in swollen joints (1). An in-vitro microbiological study (2) showed that the minimum inhibitory concentrations (MICs) of tiamulin against both MHR and *M. hyopneumoniae* (MHP) were very low.

It was the purpose of this paper to look at the pharmacokinetic (PK) and pharmacodynamic (PD) relationships of tiamulin against mycoplasmal isolates from Thailand.

Materials and methods

Pharmacodynamics: The MIC 50 and MIC 90 values for tiamulin against 20 recent Thai isolates of MHP and MHR were reported (2).

Table 1. Susceptibility of 20 recent Thai MHP and MHR isolates to tiamulin

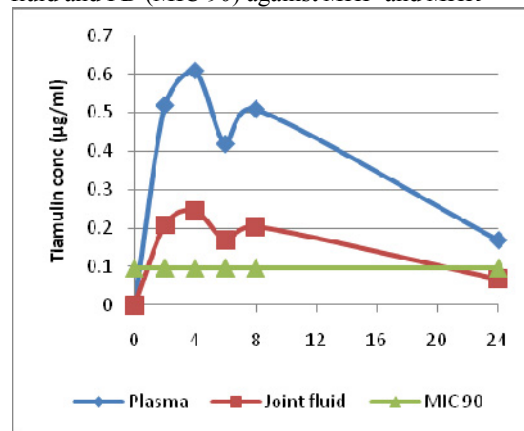
Species	MIC 50 (µg/ml)	MIC 90 (µg/ml)	MIC range (µg/ml)
MHP	0.048	0.097	0.048-0.19
MHR	0.097	0.097	0.048-0.097

Pharmacokinetics: Tiamulin distributes well into joint fluid after intramuscular administration. The concentrations achieved in plasma and joint fluid following an injection of Denagard 20% at 15mg/kg bodyweight was described (3, 4 & 5). Peak concentrations (C_{max}) of tiamulin in plasma were recorded as 0.61µg/ml (4) and that, on average, concentrations in joint fluid were approximately 40% of plasma concentration (3 & 5) (Ref Figure 1).

Results and discussion

The correlation between plasma and joint fluid concentrations with the MIC 90 of MHP and MHR at 0.097µg/ml are highlighted in Figure 1.

Fig 1. Correlation of tiamulin PK in plasma and joint fluid and PD (MIC 90) against MHP and MHR



There is a good PK correlation with tiamulin concentrations in plasma exceeding the tiamulin MIC 90 for MHP over a 24 hour period. The recommended treatment interval is 3 applications over 3 consecutive days. Tiamulin concentrations in joint fluid are somewhat lower, but appear to cover 21 hours of the 24 hour (87.5%) dosing period at the MIC 90 concentration. Many bacteriostatic antibiotics, which exert a concentration-related effect on the ribosome and thereby inhibit protein production, demonstrate a post-antibiotic effect (PAE) inhibiting bacterial re-growth for several hours (6) after plasma or tissue concentrations decline. This is likely to be the case for tiamulin against MHR.

Denagard injection at 15mg/kg bwt correlates well with its indications for the treatment of both mycoplasmal pneumonia and arthritis.

References

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