

New sensitivity test results from Professor L. Stipkovits, Hungary reported at IPVS Congress, Hamburg 2004

“Take home” messages

- Current porcine respiratory syndromes e.g. Porcine Respiratory Disease Complex (P.R.D.C.) are characterised by the multiple microbial involvement of viruses, mycoplasma and bacteria.
- *M. hyopneumoniae* is a highly significant primary pathogen in PRDC and bacteria such as *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Bordetella bronchiseptica* and *Streptococcus suis* also often play an important role.
- Tiamutin has been demonstrated in recent in-vitro studies conducted by Professor L. Stipkovits and colleagues in Hungary to be more active against *M. hyo* than a range of major competitor antibiotics – tylosin, lincomycin, CTC, tilmicosin.
- Tiamutin was demonstrated to have an enhanced antimycoplasmal/antibacterial activity when combined with doxycycline, with MIC reductions of 1.9x to 2.8x. Similarly the MIC reductions for doxycycline when deployed in combination with Tiamutin ranged from 4.9x to 9.9x.
- To successfully combat the wide range of mycoplasmal/bacterial pathogens involved in PRDC a premix combination of Tiamutin (100ppm) with either CTC (400ppm) or doxycycline (250ppm) should be a therapy of choice.

Tiamutin plus CTC or doxycycline can be effectively used to minimize the effects of both *M. hyo* and bacterial co-infections in the respiratory/enteric disease complex


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New information on the comparative in-vitro sensitivities of key porcine respiratory pathogens to Tiamutin and other antibiotics has become available from Professor L. Stipkovits in Hungary.

This was reported at the IPVS Congress in Hamburg 2004.

This information is considered below in two sections as follows:

- A) Comparative in-vitro activity of Tiamutin and other antibiotics against *M. hyopneumoniae*, *M. hyorhinis*, *A. pleuropneumoniae*, *M. hyosynoviae*, *Pasteurella multocida*, *S. suis* and *B. bronchiseptica*.
- B) In-vitro synergism between Tiamutin and doxycycline against respiratory mycoplasmal and bacterial pathogens.

- A) Comparative in-vitro activity of Tiamutin and other antibiotics against *M. hyopneumoniae*, *M. hyorhinis*, *A. pleuropneumoniae*, *M. hyosynoviae*, *Pasteurella multocida*, *S. suis* and *B. bronchiseptica*.

10 strains of each of the mycoplasma species were isolated from the tissues of pigs using Friis medium or medium B (Erno and Stipkovits). They were then cloned and identified biochemically and serologically and preserved by lyophilisation.

The identity of the *M. hyopneumoniae* strains was also confirmed by PCR.

The MIC₅₀, MIC₉₀ values and MIC range for the 6 antimicrobials were determined and are summarized in Tables 1 – 7 below.

Table 1: MIC's (µg/ml) of 10 isolates of *M. hyopneumoniae* to 6 antimicrobials

Antimicrobial	MIC range	MIC ₅₀	MIC ₉₀
Doxycycline	0.5 – 32.0	4.0	16.0
CTC	4.0 – 32.0	16.0	32.0
Tylosin	0.25 – 16.0	2.0	16.0
Tilmicosin	0.125 – 2.0	0.25	2.0
Lincomycin	0.25 – 8.0	2.0	8.0
Tiamulin	0.06 – 1.0	0.25	1.0



Table 2: MIC's ($\mu\text{g/ml}$) of 10 isolates of *M. hyorhinis* to 6 antimicrobials

Antimicrobial	MIC range	MIC ₅₀	MIC ₉₀
Doxycycline	0.06 – 8.0	0.5	8.0
CTC	4.0 – 32.0	16.0	32.0
Tylosin	4.0 – 32.0	8.0	32.0
Tilmicosin	0.5 – 8.0	2.0	8.0
Lincomycin	1.0 – 8.0	2.0	8.0
Tiamulin	0.06 – 2.0	0.125	1.0

Table 3: MIC's ($\mu\text{g/ml}$) of 10 Hungarian field isolates of *Actinobacillus pleuropneumoniae* (App) to 6 antimicrobials

Antimicrobial	MIC range	MIC ₅₀	MIC ₉₀
Doxycycline	0.25 – 8.0	0.25	1.0
CTC	1.0 – 32.0	8.0	32.0
Tylosin	4.0 – 32.0	16.0	32.0
Tilmicosin	0.5 – 2.0	2.0	2.0
Lincomycin	1.0 – 16.0	8.0	16.0
Tiamulin	2.0 – 4.0	2.0	4.0

Though less active than doxycycline and tilmicosin, tiamulin was superior to the remaining antibiotics tested. It should be noted that tiamulin shows a marked synergism against App when combined with doxycycline.

(See section (B) below)

Table 4: MIC's 1 ($\mu\text{g/ml}$) of 10 isolates of *M. hyosynoviae* to 6 antimicrobials

Antimicrobial	MIC range	MIC ₅₀	MIC ₉₀
Doxycycline	0.25 – 4.0	1.0	2.0
CTC	8.0 – 32.0	8.0	32.0
Tylosin	2.0 – 32.0	4.0	16.0
Tilmicosin	2.0 – 32.0	4.0	16.0
Lincomycin	0.5 – 8.0	2.0	4.0
Tiamulin	0.03 – 0.25	0.125	0.25

On the basis of the MIC range, MIC₅₀ and MIC₉₀ values, tiamulin again showed a superior potency to other antibiotics tested.

Table 5: MIC's ($\mu\text{g/ml}$) of 10 field isolates of *Pasteurella multocida* to various antimicrobials

Antimicrobial	Range	MIC ₅₀	MIC ₉₀
Doxycycline	0.03 – 0.5	0.125	0.25
CTC	1.0 – 32.0	8.0	16.0
Tylosin	2.0 – 32.0	16.0	32.0
Tilmicosin	0.125 – 2.0	1.0	2.0
Lincomycin	8.0 – 32.0	16.0	16.0
Tiamulin	1.0 – 8.0	2.0	4.0

Doxycycline was shown to possess highly potent activity versus *Pasteurella multocida*. Tiamulin shows a marked synergism against *P. multocida* when combined with doxycycline.

(See section (B) below)

Table 6: MIC's ($\mu\text{g/ml}$) of 10 field isolates of *Streptococcus suis* to various antimicrobials

Antimicrobial	Range	MIC ₅₀	MIC ₉₀
Doxycycline	0.125 – 8.0	0.125	0.125
CTC	8.0 – 32.0	8.0	16.0
Tylosin	0.06 – 0.5	0.125	0.25
Tilmicosin	0.03 – 2.0	1.0	2.0
Lincomycin	0.03 – 2.0	0.5	0.5
Tiamulin	0.015 – 0.5	0.125	0.25

Tiamulin was demonstrated, along with tylosin, to be highly active against *S. suis*.

Table 7: MIC's ($\mu\text{g/ml}$) of 10 field isolates of *Bordetella bronchiseptica* to various antimicrobials

Antimicrobial	Range	MIC ₅₀	MIC ₉₀
Doxycycline	0.06 – 0.125	0.06	0.125
CTC	1.0 – 32.0	4.0	32.0
Tylosin	2.0 – 32.0	32.0	32.0
Tilmicosin	1.0 – 8.0	4.0	8.0
Lincomycin	16.0 – 32.0	32.0	32.0
Tiamulin	8.0 – 32.0	16.0	32.0



B) In-vitro synergism between Tiamulin and doxycycline against respiratory mycoplasmal and bacterial pathogens.

Doxycycline is a semi-synthetic long-acting tetracycline derivative which appears to offer important advantages over earlier tetracyclines.

Its major advantage is greater lipid solubility, which probably accounts for its enhanced antimicrobial effects, more efficient absorption following oral administration and enhanced distribution in the body. The penetration of doxycycline into the lung tissues, bronchial wall and bronchial secretions is good.

Organism	Average MIC's (µg/ml)				Synergy factor	
	Tiamulin	Doxycycline	Combined Tia/Doxy		Tia	Doxy
			Tia	Doxy		
<i>M. hyopneumoniae</i>	0.219	5.169	0.094	0.659	2.3x	7.8x
<i>M. hyorhinis</i>	0.219	0.933	0.116	0.094	1.9x	9.9x
<i>A. pleuropneumoniae</i>	2.297	0.435	1.071	0.088	2.1x	4.9x
<i>P. multocida</i>	2.297	0.125	0.870	0.016	2.6x	7.8x
<i>S. suis</i>	0.094	0.189	0.044	0.025	2.1x	7.6x
<i>B. bronchiseptica</i>	16.0	0.088	5.656	0.017	2.8x	5.2x
<i>M. hyosynoviae</i>	0.120	1.101	0.044	0.116	2.7x	9.5x

Using the combination of tiamulin with doxycycline a remarkable enhancement of antimycoplasmal/antibacterial activity was observed, varying from 1.9x to 2.8x for tiamulin and from 4.9x to 9.9x for doxycycline.

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Further information on the Tiamulin® (tiamulin) range of products is available from the Pig Products Manager at Novartis Animal Health operations in over 50 countries worldwide.

References

1. Stipkovits, L. and others (2004) Proc. 18th IPVS Congress, Hamburg, Germany. Vol 2. p518.
2. Fodor, L. and others (2004) Proc. 18th IPVS Congress, Hamburg, Germany. Vol 2. p563.