

# PK/PD and clinical relationships of Pharmasin® Water Soluble Granules (tylosin tartrate) administered to pigs for the treatment of Necrotic Enteritis

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## Background and Objectives

The pharmacokinetics (PK) of tylosin tartrate (Pharmasin® - Huvepharma NV) colon content concentration (CCC) based on water medication was related to tylosin MICs against *Clostridium perfringens* (CP) Type A strains (pharmacodynamics - PD).

## Materials and Methods

The tylosin CCC was determined in a PK study with eleven pigs (bodyweight 20-25kg), which were medicated at a dose of 10mg/kg bw.<sup>1</sup> Medicated water was offered ad libitum (5 consecutive days).

On day 5 of the PK study pigs were euthanized at 5 different time points. Tylosin PK parameters (AUC<sub>0-12h</sub> µg.h/g; T<sub>max</sub> h; C<sub>max</sub> µg/g; AUC µg.h/g/hour) were determined. AUC per hour (AUC µg.h/g/hour) was calculated to determine the tylosin CCC at registered (5-10mg/kg =100-200ppm) enteric infection treatment dose for water medication.

Tylosin MIC data were generated based on susceptibility testing of *Clostridium perfringens* toxinotype A strains in an Italian and a Brazil study.<sup>2,3</sup> 51 CP Italian and 50 CP Brazil strains were MIC tested (MIC dilutions: 0.06 - 512 µg/ml). The MIC<sub>50</sub>, MIC<sub>90</sub> and MIC ranges were determined.



## Results

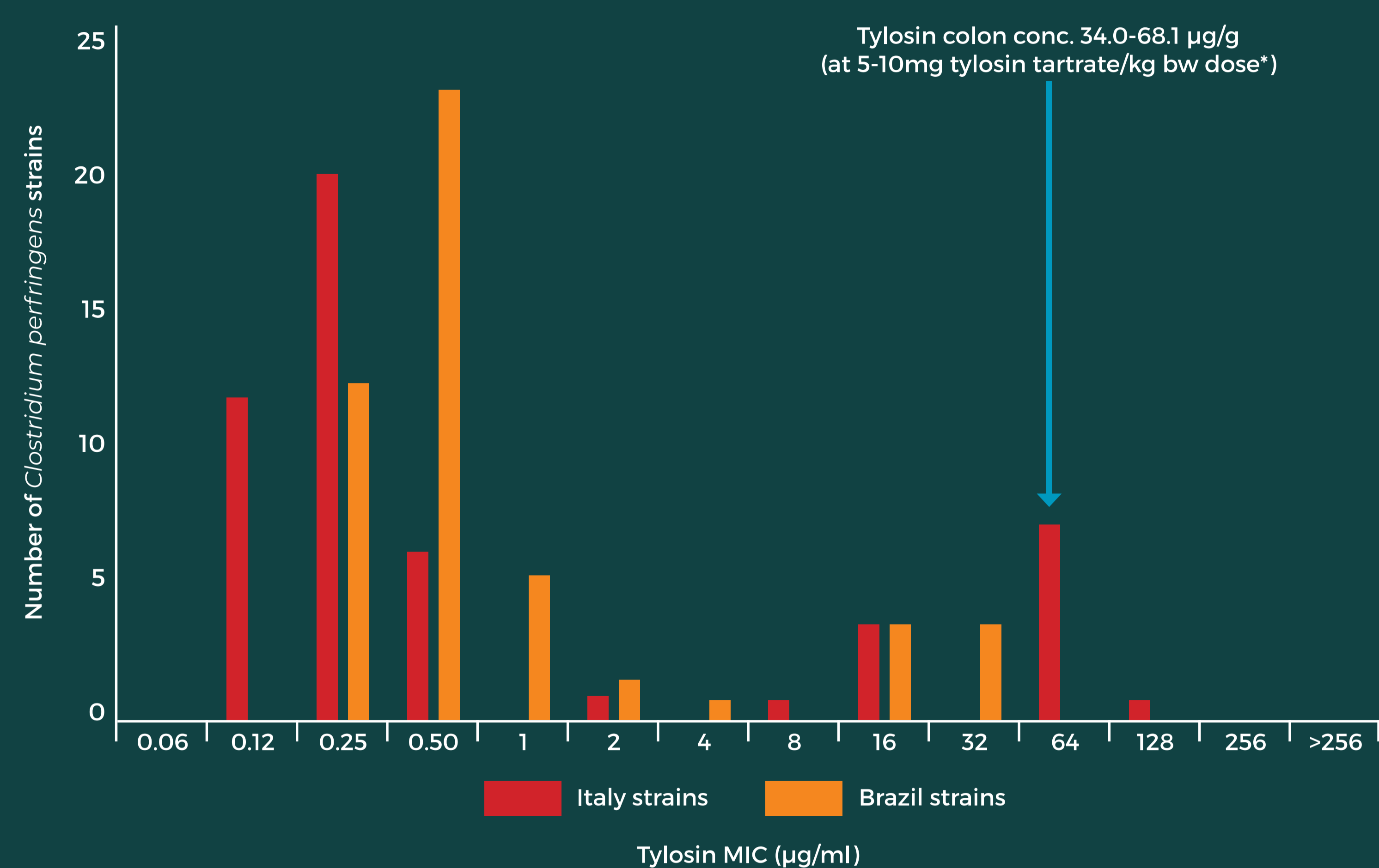
The tylosin CCC AUC<sub>0-12h</sub> µg.h/g at 10mg tylosin tartrate/kg bw was recorded at 816.85 after water medication. The CCC per hour was estimated (E) at 34.0µg/g and 68.1µg/g at registered water medication dose range of 5-10mg/kg bw. In the Italian MIC study tylosin MIC<sub>90</sub> values of 64µg/ml and MIC range of 0.125-128µg/ml were measured. A tylosin MIC<sub>90</sub> value of 16µg/ml and MIC range of 0.25-32µg/ml were determined for the Brazil CP strains. PK/PD relationships show that tylosin CCC's are high and exceed the MIC values of all Brazil and 85% of the tested Italian CP strains.

**Table 1.** Tylosin pharmacokinetics - estimated tylosin colon content concentrations following administration at 2 registered dose levels in drinking water

Parameter unit	Colon contents (µg.h/g)	Colon contents (average conc µg.h/g/hour) : tylosin dosage 10mg/kg bw	Colon contents (average conc µg.h/g/hour) : tylosin dosage 5mg/kg bw
AUC <sub>0-12h</sub> µg.h/g	816.85	E 68.1	E 34.0

**Table 2.** MIC ranges, MIC<sub>50</sub> and MIC<sub>90</sub> (µg/ml) of tylosin for *Clostridium perfringens* strains from Italy and Brazil

Publication / report	Region	N strains	MIC range	MIC <sub>50</sub>	MIC <sub>90</sub>
Agnoletti, F. 2021	Italy	51	0.125-128	0.25	64
Salvarani, F.M. et al. 2012	Brazil	50	0.25-32	0.5	16



\*Pharmasin® registered treatment dose enteric diseases: 5-10mg tylosin tartrate/kg bw

**Figure 1.** Tylosin PK/PD relationships for *Clostridium perfringens* strains from Italy and Brazil

## Conclusion

An excellent therapeutic and metaphylactic effect of tylosin tartrate in the case of oral *Clostridium perfringens* infection treatment via water medication can be expected based on available PK/PD data.

## References

- Vesselova S. et al. (2010). PK and PK/PD of Pharmasin® 100% W/W (tylosin tartrate) following multiple oral administration in pigs. Proceedings 21<sup>st</sup> IPVS Congress, Vancouver, Canada, p.992.
- Agnoletti, F. (2021). Drug susceptibility of *Clostridium perfringens* field strains isolated from swine. Istituto Zooprofilattico Sperimentale delle Venezie, final report.
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