



Flavomycin[®]

Flavomycin[®] decreases antibiotic resistance

1. Flavomycin[®] decreases antibiotic resistance

Antibiotic resistance can be acquired via transfer of extrachromosomal DNA located on plasmids. Those plasmids are called R-factors and can encode for multiple drug resistance. Plasmids pass from one bacterium to another through bacterial conjugation (pilus) (Fig 1).

Fig 1 without Flavomycin[®]

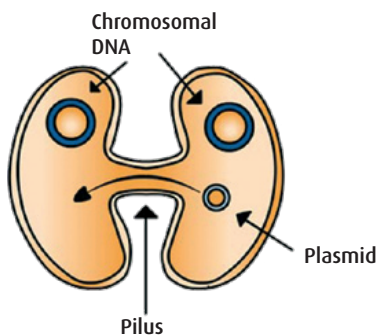
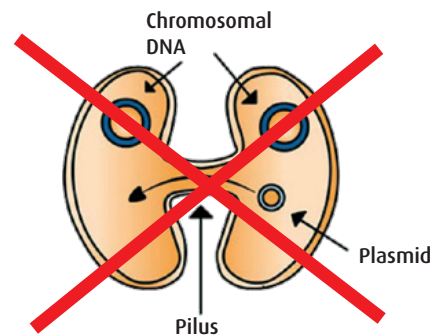


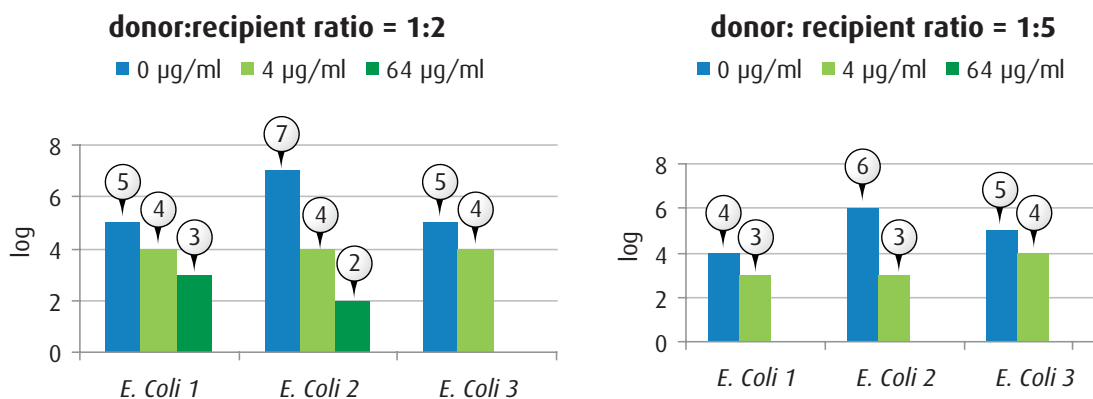
Fig 2 with Flavomycin[®]



Flavomycin[®] decreases antibiotic resistance by

1. Reducing the conjugation transfer of plasmids (Fig 2)
2. Having enhanced activity against plasmid containing bacteria = plasmid curing effect

Below the conjugation efficiency of 3 broad spectrum beta lactamase *E. coli* plasmids are depicted for various Flavomycin[®] concentrations.



Flavomycin[®] reduces the horizontal spread of plasmids under high and low resistance pressure.

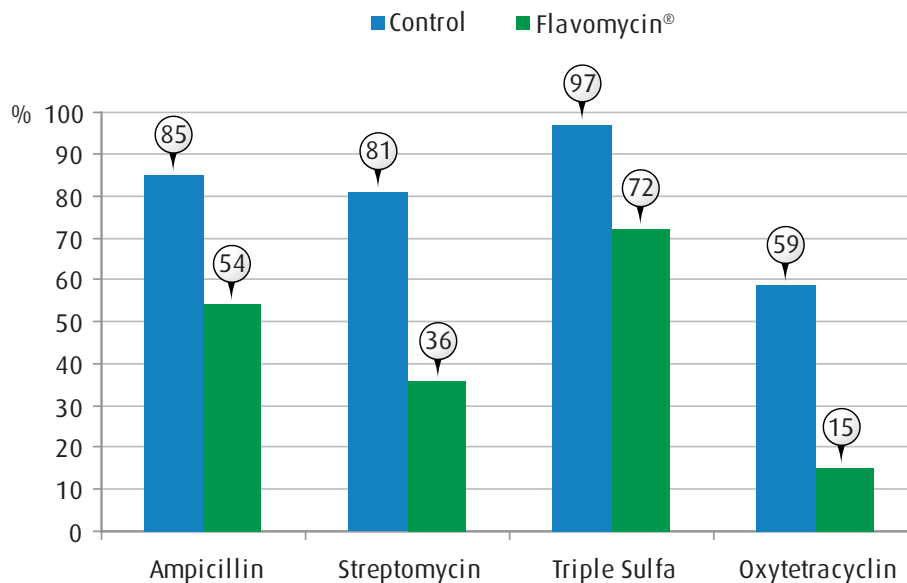
2. Trials

2.1 Flavomycin® decreases the antibiotic resistance of *Salmonella* spp.

Trial:

- 6 - weeks old pigs inoculated with 2.5×10^{11} multi resistant *Salmonella typhimurium*
- Treatments: - negative control: 10 pigs
- Flavomycin® 4.4 ppm: 10 pigs
- Faeces samples at 21 days post infection
- *Salmonella* susceptibility was tested

Percentage of pigs with *Salmonella* resistant strains 21 days post infection



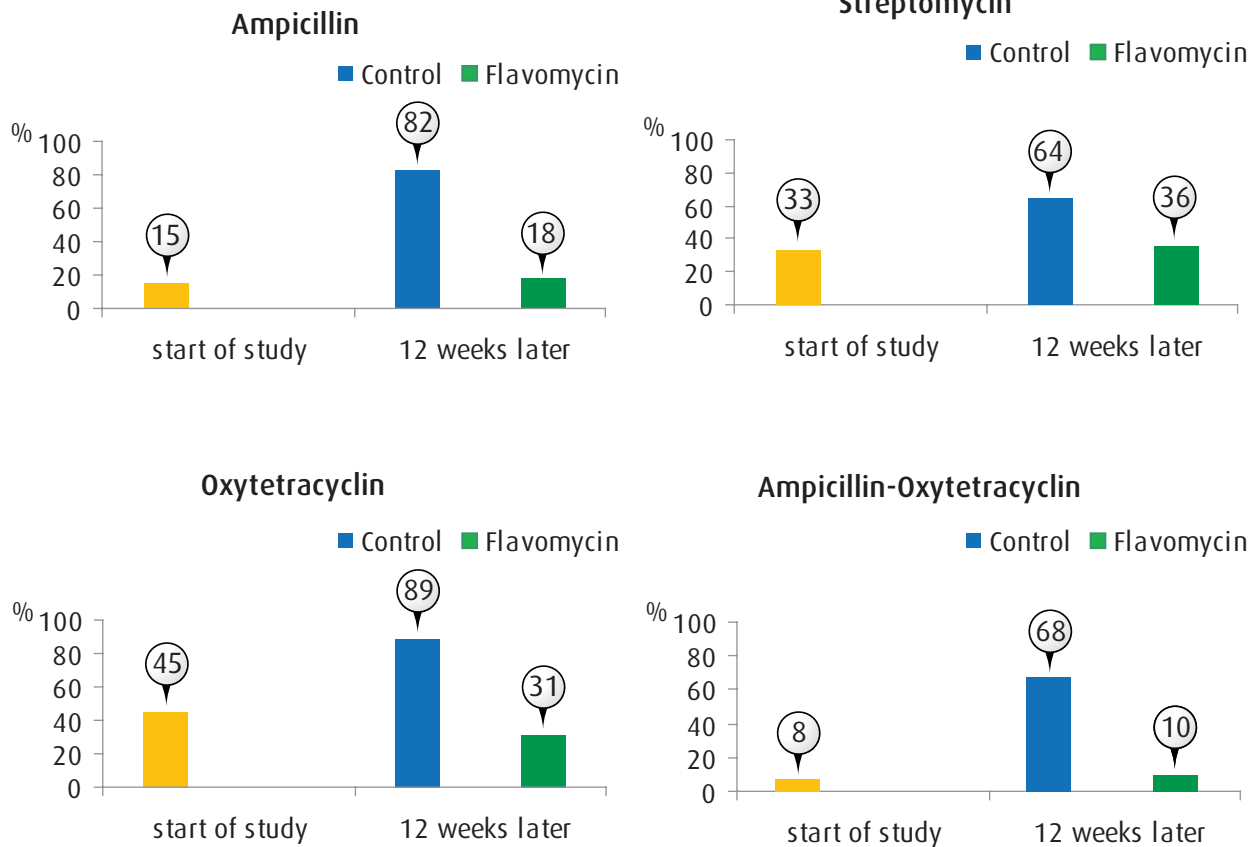
Flavomycin® reduces the number of pigs carrying multi-drug resistant *Salmonella*.

2.2 Flavomycin® decreases the antibiotic resistance of *E. Coli*

Trial:

- Fattening pigs inoculated with three multi resistant nonpathogenic *E. Coli* strains
- Treatments: - negative control: 56 pigs
- Flavomycin® 9 ppm: 56 pigs
- Faeces samples before infection and 12 weeks post infection
- *E. Coli* susceptibility was tested

Percentage of resistant *E. Coli* at the start of the study and 12 weeks later



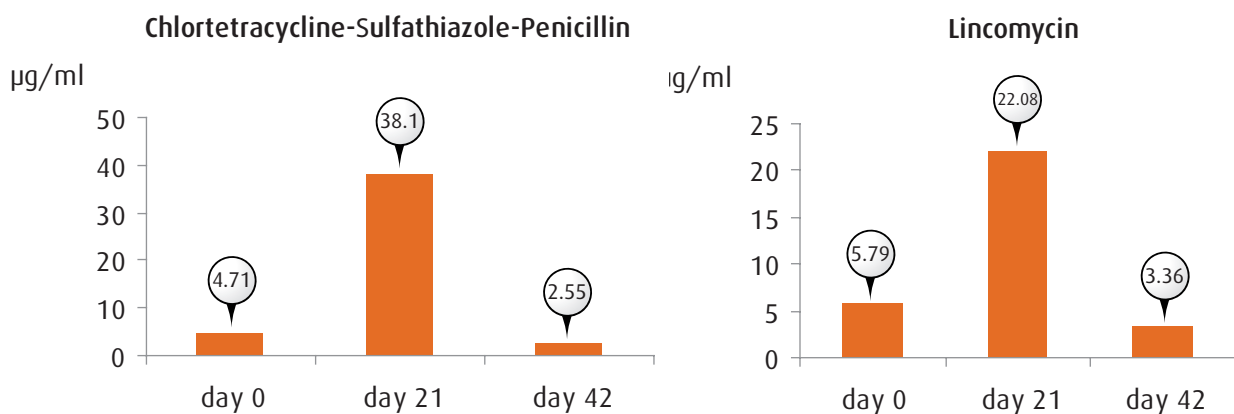
Flavomycin® reduces the number of multiple drug resistant *E. Coli*.

2.3 Flavomycin® reverses previously generated antibiotic resistance

Trial:

- 20-weeks old pigs
- Day 0 till day 21 of study:
 - Chlortetracyclin-Sulfathiazole-Penicillin (100-100-50 ppm): 30 pigs
 - Lincomycin (100 ppm): 30 pigs
- Day 21 till day 42 of study:
 - stop antibiotic treatment: all pigs
 - start Flavomycin® 4 ppm: all pigs
- Faeces samples day 0, 21 and 42 of the study
- MIC-values for *E. Coli* against Ampicillin were tested

MIC-values for *E. Coli* against Ampicillin from pigs previously exposed to antibiotic treatment



Flavomycin® reverses MIC-values increased by antibiotic treatment.

3. Characteristics of Flavomycin®

- No acquired resistance against Flavomycin®
- Exposure of bacteria to Flavomycin® does not result in cross-resistance
- Flavomycin® is used solely as a feed additive
- Flavomycin® has no therapeutic use in humans
- The unique mode of action of Flavomycin® is not shared by any agent used in human medicine

Conclusions

Flavomycin®:

- reduces conjugation transfer of plasmids
- has enhanced activity against plasmid containing bacteria
- reduces antibiotic resistance of *Salmonella spp.*
- reduces antibiotic resistance of *E. Coli spp.*
- reverses previously generated antibiotic resistance
- causes no resistance or cross-resistance