Intestinal concentrations of sulfadiazine-trimethoprim in pigs after oral and intramuscular treatment

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Introduction

Dosage regimens of antimicrobials in animal husbandry commonly show considerable variability, this can lead to differences in plasma and intestinal concentrations. These differences can have consequences on the occurrence of resistance selection. Therefore the effect of an oral versus intramuscular (I.M.) treatment on these concentrations was investigated. This study focuses on sulfadiazine-trimethoprim (SDZ-TRIM), an antimicrobial combination often used in the oral and I.M. treatment of pigs.

Following objectives were outlined:
- To develop and validate a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method to quantify SDZ-TRIM in plasma and intestinal content of pigs.
- To evaluate intestinal concentrations of SDZ-TRIM combination after oral as well as I.M. administration in pigs, using conventional dosing and dose alteration.

Materials & Methods

Quantitative analysis of plasma and intestinal samples:
- Sample preparation (Fig.1) using liquid-liquid extraction with ethyl acetate (EtOAc).
- LC-MS/MS analysis using trimethoprim-d5 and sulfadiazine-13C as internal standards.
- The mass spectrometer was equipped with a heated electrospray ionization in positive mode.

Animal study: 36 pigs (mixed genders, aged ten weeks) randomly divided into six different treatment groups (n=6):
- Five consecutive days of treatment.
- Daily collection (every twelve hours) of fecal and blood samples. Fecal samples were collected after spontaneous excretion or via rectal stimulation.
- Twelve hours after final administration of SDZ-TRIM: euthanasia and collection of intestinal contents in five gut segments (duodenum, jejunum, ileum, cecum, colon and rectum).

Results & Conclusions

The LC-MS/MS method was validated using matrix-matched samples for plasma, feces and intestinal content. The limit of quantification was 25 ng/mL in plasma and 25 ng/g in feces for both compounds.

Above preliminary results of the animal study are illustrated, based on one pig per group. These data however already reveal a clear trend, namely TRIM that is present in fecal samples to a much lesser extent than SDZ. Based on the SDZ-TRIM concentrations in the different intestinal segments, found after 108 hours of therapy (Fig 4: only pig 1 from group 2 shown), trimethoprim concentrations appear to decrease rapidly going further down the gut. On the other hand sulfadiazine concentrations rather tend to increase in the colon and rectum segments. This implies the presence of a degradation mechanism for TRIM, which is supported by the low fecal concentrations in comparison to SDZ (Fig 5).

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