# Antibiotic treatment affects intestinal permeability and gut microbial composition in female Wistar rats dependent on antibiotic class

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# Antibiotic treatment affects intestinal permeability and gut microbial composition in female Wistar rats dependent on antibiotic class

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## Introduction

Antibiotics are frequently administered orally to treat both systemic and localized bacterial infections in almost any body location. As a consequence of this, the commensal gut microbiota is very often affected as well. This may disrupt the normal balance and subsequently affect intestinal integrity and host health.

## Methods

Female Wistar rats (n=60) were dosed with amoxicillin (AMX), cefotaxime (CTX), vancomycin (VAN), metronidazole (MTZ), or water (CON) every day for 10-11 days (n=12 in each group). Changes in bacterial composition in faecal and caecal content were determined by partial sequencing of the 16S rRNA gene. Intestinal permeability was determined in vivo by measuring permeability of 4kDa FITC-dextran.

## Results

Intestinal permeability was increased by administration of MTZ, while CTX and VAN decreased intestinal permeability. Bacterial composition and alpha diversity was significantly influenced by AMX, CTX and VAN but not by MTZ. In all groups with significant changes compared to CON, Firmicutes was reduced while Bacteroidetes and Proteobacteria were increased. For CTX abundance of Bifidobacteriaceae in the caecum content increased significantly while in the VAN group Lactobacillaceae increased in both caecal and faecal samples. Administration of AMX, CTX and MTZ resulted in increased water intake, while only AMX affected feed intake. Caecum weight was increased by AMX and VAN and the latter also increased caecum pH.

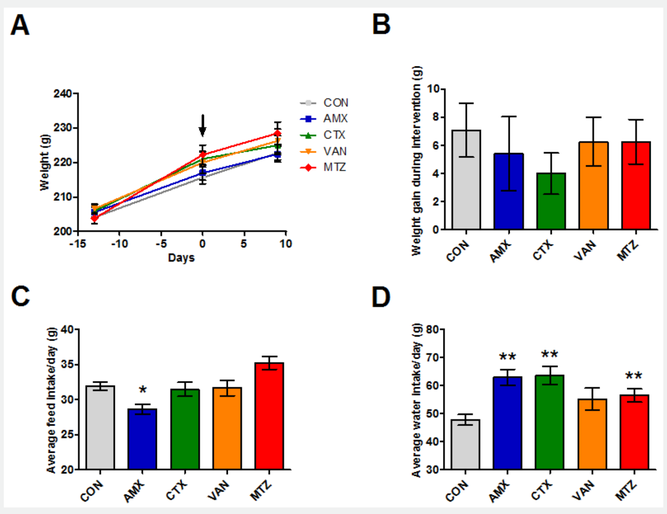


**Figure 1. Animal weight, food and water intake.** (A) Mean animal weight during the acclimation and intervention period. The arrow indicates the initial dosing. No significant differences were determined between the CON and either of the treatments at day -13, 0 and 9 according to a two-way ANOVA. (B) Mean weight gain during the intervention with antibiotics (day 0 to 9). (C) Mean feed intake per day during the intervention period and (D) mean water intake per day during the intervention. Bars show averages for each group and error bars show SEM. Significant differences from CON group are indicated by asterisks (*; P < 0.05, **; P < 0.01).

**Figure 2: Characteristics of cecum.** (A) Weight of caecum and (B) pH in caecum. Each point represents an individual animal. Horizontal lines and error bars show means and SEM, respectively. Significant differences from CON group are indicated by asterisks (*; P < 0.05, **; P < 0.01).

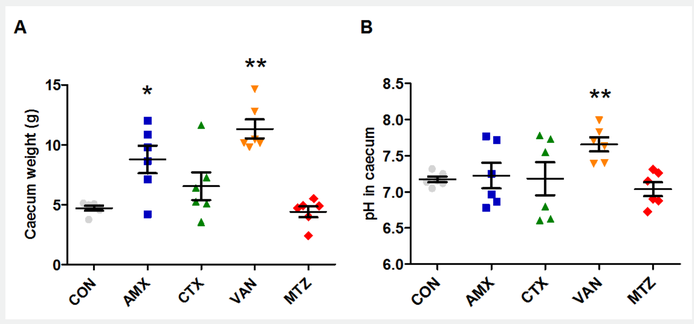



**Figure 3. Size of caecum**. Representative photographs of a caecum from an animal in the CON group (5.06 g) and from the VAN group (10.14 g).

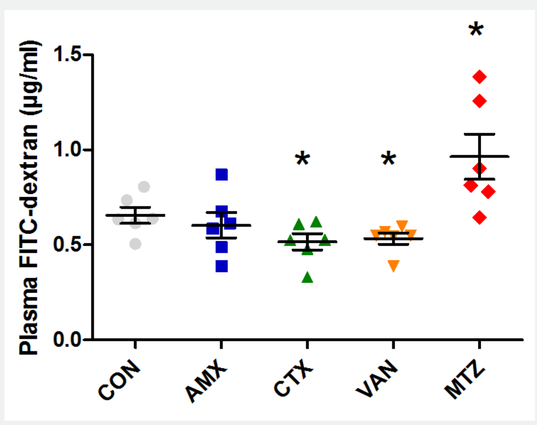


**Figure 4: Plasma FITC-dextran concentrations.** Each point represents an individual animal. Horizontal lines and error bars show means and SEM, respectively. Significant differences from CON group are indicated by asterisks (*; P < 0.05).

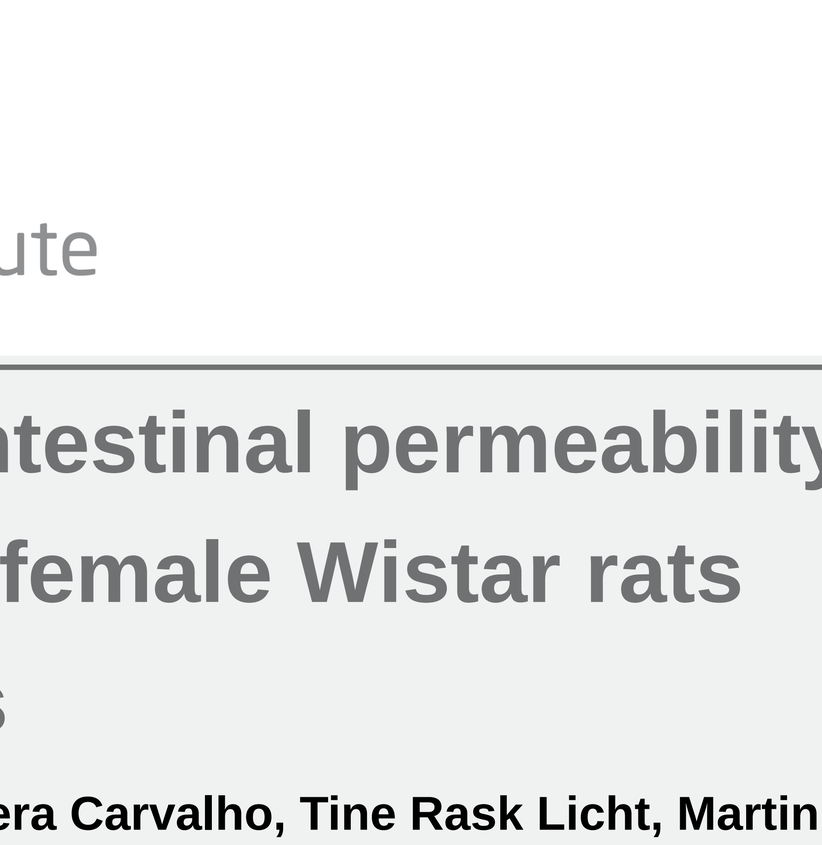


**Figure 5. Bacterial community composition in faeces and caecum content samples based on 16S rRNA gene sequencing.** The mean bacterial composition is shown at the family level for faecal samples (day 0 and 10) and caecal content samples for animal in CON, AMX, CTX, VAN and MTZ groups. The most abundant bacterial phyla are represented by Firmicutes (blue colors), Bacteroidetes (red colors), Proteobacteria (green colors), Actinobacteria (yellow colors), and unclassified bacteria (black).

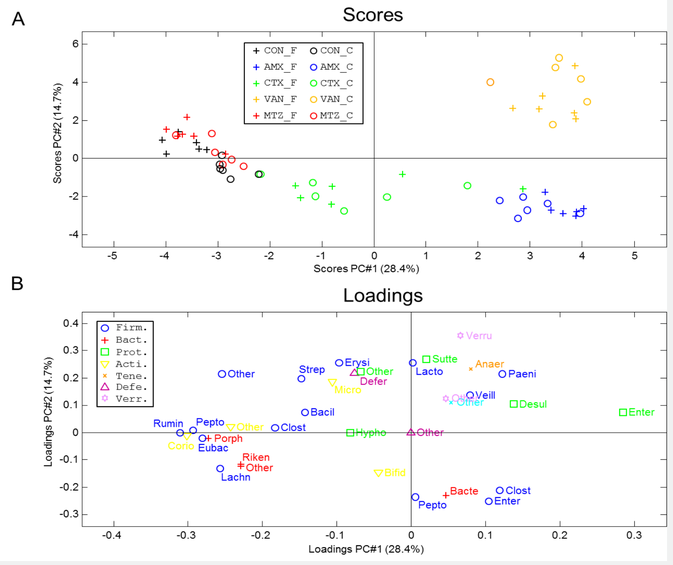


**Figure 6: Principal component analysis (PCA) of the relative abundances of detected bacterial families in faecal and caecal samples.** (A) The score plot shows samples grouped according to treatment groups CON (black), AMX (blue), CTX (green), VAN (yellow) and MTZ (red) groups, with six animals in each group. ○: Cecal samples; +: Feces samples. (B) Loading plot indicating each of the bacterial families colored according to phylum. Firm, Firmicutes (blue); Bact, Bacteroidetes (red); Prot, Proteobacteria (green), Acto, Actinobacteria (yellow); Tene, Tenericutes (orange); Defe, deferribacteres (pink) and Verr, Verrucomicrobia (light pink).

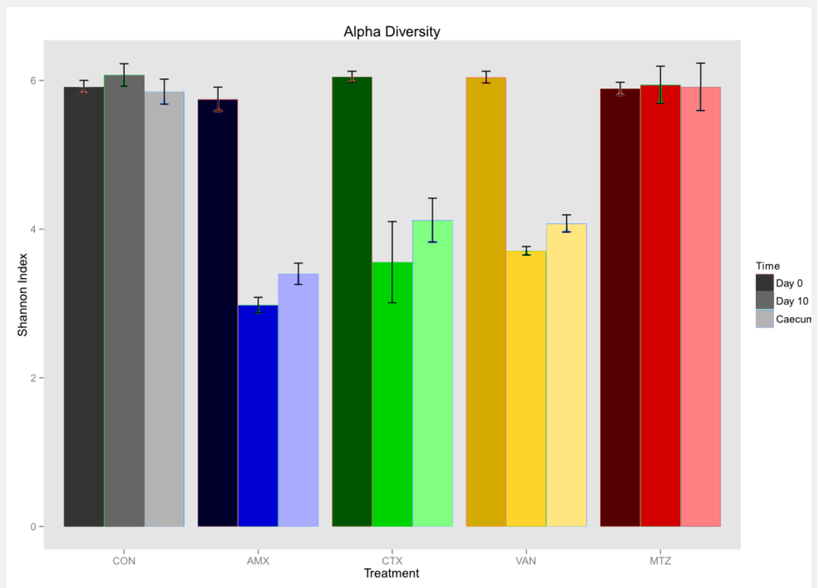


**Figure 7: Alpha diversity plot of faecal samples before and after AB treatment and caecal samples.** Before AB treatment all faecal samples showed similarly high alpha diversity. After AB treatment alpha diversity in faecal and caecal samples is lower in most groups apart from MTZ (red) group. In each group are the samples as follows. Darkest color, left: Fecal samples before AB treatment; Middle column: Faeces after 10 Days of treatment; Lightest color, right: caecum sample.

## Conclusion

Specific antibiotics were shown to affect intestinal permeability in either a positive or negative direction dependent on the class of antibiotic. Changes in gut microbial composition and alpha diversity, which were also observed, could be linked to intestinal permeability, although changes in permeability did not always result from major changes in microbiota and vice versa.

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