

Comparison of the effect of fidaxomicin, thuricin CD, vancomycin and nisin on the human gut microbiota, both in vitro and ex vivo.

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Introduction: Vancomycin and metronidazole are commonly used treatments for *Clostridium difficile* infection (CDI). However, these antibiotics have been associated with high levels of relapse in patients. A new treatment for CDI, fidaxomicin, is described as a narrow spectrum antibiotic that is minimally active on the commensal bacteria of the gut microbiome. The aim of this study was to investigate the effect of fidaxomicin on the human gut microbiome and to compare it to thuricin CD, vancomycin and nisin.

Methods: The spectrum of activity of each antimicrobial was tested against 50 bacterial strains, including a variety of antibiotic resistant and gut strains, by well diffusion assay. MIC's were performed for each antimicrobial against a select number of those strains. The micro-Matrix™ mini fermentation system was used to simulate the environment of the colon. A pooled faecal slurry of 6 donors with 100µM of each antimicrobial and a no treatment control was assessed in the mini-fermentation system.

Results: Fidaxomicin, vancomycin and nisin were active against most Gram-positive bacteria tested, although fidaxomicin and vancomycin produced larger zones of inhibition. In contrast, activity of thuricin CD was specific to *C. difficile* and some Bacillus strains. Thuricin CD exhibited low MIC's for *C. difficile* and *B. firmus*. Whereas, fidaxomicin, vancomycin and nisin demonstrated lower MIC's for other strains tested when compared to thuricin CD. These results were mirrored in the micro-Matrix™ system.

Discussion: We conclude that the spectrum of activity of fidaxomicin is comparable to that of the broad spectrum antibiotic vancomycin, and is therefore broad spectrum. While active against *C. difficile*, fidaxomicin does show activity against gut commensal bacteria such as Bifidobacterium, Ruminococcus and some Lactobacillus strains, unlike thuricin CD which is very narrow spectrum.