Background: Antibiotic-associated diarrhea is caused by S. aureus (SA) and C. difficile (CDIF) with increased morbidity and mortality in recent years, with oral vancomycin (VAN) and/or metronidazole as the preferred treatment. Since antibiotic treatment can have side effects while a patient is on other therapies, it is possible that non-antibiotic therapeutic agents could interact with or even enhance the antibacterial activity. The objective of the presented study was to screen for potential antagonistic interactions between vancomycin and selected non-antibiotic agents.

Methods: Three SA strains and seven CDIF isolates were tested against a selected group of 13 non-antibiotic agents (NATA) with log2 dilutions of a NATA, ranging from 10,000 to 31 µg/ml, or from 1,000 to 1,000 µg/ml with and without VAN. The absence of growth when the NATA was tested alone indicated anti-SA activity while the presence of growth when the NATA was tested with VAN showed antagonism. Three CDF strains were tested against a selected group of 13 NATA compounds using an agar dilution method.

Results: For SA30-20C No 25, VAN showed antagonism. Three SA strains with reproducible activity at low levels (25 – 100 µg/ml; 1,000 – 2,000 µg/ml; 10,000 µg/ml) were tested over a range of eight concentrations beginning at 1 µg/ml. The absence of growth when the non-antibiotic therapeutic agent compounds when combined with vancomycin showed antagonism. Three C. difficile strains were tested against a selected group of 13 non-antibiotic therapeutic agents using an agar dilution method according to Clinical and Laboratory Standards Institute (CLSI; M11-A7) recommendations. Each SA strain was tested over a range of eight concentrations beginning with 2,000 µg/ml (0.2% of full potency) except for folic acid, which started at 1,000 µg/ml (11%), using log2 dilutions of 2,000; 1,000; 500; 250; 125; 63; 31 and 16 µg/ml or 0.125; 0.062; 0.031; 0.016 µg/ml. The antibacterial activities of several non-antibiotic therapeutic agents against S. aureus were only observed at extremely high concentrations.

Conclusions: No antagonism of vancomycin activity was observed against C. difficile with any of the non-antibiotic therapeutic agents evaluated. The antibacterial activities of several non-antibiotic therapeutic agents against S. aureus (MIC, 25 to 100,000 µg/ml) or C. difficile (MIC, 31 to 2,000 µg/ml) strains warrant further evaluation.