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P1679 Resensitizing the antibiotic aztreonam using the polyphenol epigallocatechin gallate against multidrug-resistant clinical isolates of Pseudomonas aeruginosa and Acinetobacter baumannii

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Background: *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are important nosocomial pathogens; frequently associated with severe and difficult to treat infections; often innately multidrug-resistant (MDR) and linked to high rates of morbidity and mortality. With insufficient anti-Gram-negative antibiotics under development, novel therapies/combinations are urgently required, to support existing drugs, or to increase their lifespan. One such option would be to use polyphenols, such as epigallocatechin gallate (EGCG), which has previously shown to have antibacterial activity alone and in combination with licenced antibiotics. This study aimed to determine if EGCG was able to resensitize aztreonam against MDR strains of *P. aeruginosa* and *A. baumannii.*

Materials/methods: Minimum inhibitory concentrations (MICs) of aztreonam, EGCG and combinations of both agents were performed against MDR clinical isolates of *P. aeruginosa* (n = 17) and *A. baumannii* (n = 17). All strains were deemed susceptible/intermediate/resistant, based on European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints for *Pseudomonas spp.* All assays were performed in triplicate. Kill-kinetic assays were performed over 24 h to confirm antibacterial activity of aztreonam alone and in combination with EGCG.

Results: Results from MIC testing showed that sixteen strains of *P. aeruginosa* were resistant to aztreonam and one isolate was susceptible. Fifteen *A. baumannii* strains were resistant to aztreonam and two intermediately resistant. However, when used in combination with EGCG, aztreonam susceptibility increased in *P. aeruginosa* (n = 16) and *A. baumannii* (n = 13). The combination proved synergistic in all, but one strain of *P. aeruginosa* (FICIs = 0.02-0.5). Kill-kinetic assays confirmed synergy (>3 logs reduction in CFU/mL) between aztreonam and EGCG with the combination producing bactericidal activity over 24 h. The combination was significantly more active (*P* = <0.05) than either agent alone at 24 h.

Conclusions: The results from this study not only demonstrate that synergy exists between aztreonam and EGCG against MDR clinical strains of *P. aeruginosa* and *A. baumannii,* but EGCG is able to resensitize aztreonam to concentrations below the EUCAST susceptibility breakpoint. This combination has the potential to treat infections caused by MDR *P. aeruginosa* and *A. baumannii*.