Design of a Multi-Mechanistic Triple Therapy to Overcome Biofilm-Associated Resistance in Pseudomonas aeruginosa

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Biofilm-mediated resistance is a major barrier to treating Pseudomonas aeruginosa infections. Biofilms are estimated to contribute to over 65% of microbial infections, allowing bacteria to persist despite antibiotics and host immune defenses and driving chronic, multidrug-resistant disease. This study investigates the relationship between biofilm formation and antimicrobial resistance (AMR) gene expression in P. aeruginosa and evaluates a triple-therapy strategy combining resveratrol, EDTA, and meropenem. Fifty clinical isolates were analyzed. Biofilm production was quantified using the crystal violet microtiter assay (OD550), antimicrobial susceptibility was assessed via VITEK-2, and key AMR genes (mexB, ampC, gyrA, and oprD) were detected using PCR. Correlation analysis assessed the relationship between biofilm biomass and resistance gene prevalence. Chequerboard assays evaluated drug interactions using fractional inhibitory concentration indices (FICI). Results showed substantial variability in biofilm formation, with strong producers exceeding OD550 > 2.5. Multidrug resistance was widespread, supported by efflux pump, ß-lactamase, porin, and gyrase-associated genes. A positive correlation (r = 0.22) between biofilm biomass and AMR gene count suggests that stronger biofilm formation is linked to increased resistance potential. Chequerboard testing demonstrated synergistic interactions, with reduced effective concentrations and FICI values indicating greater efficacy than monotherapy. By targeting quorum sensing, matrix stability, and cell wall synthesis simultaneously, this strategy may improve outcomes and support more effective therapy for chronic and drug-resistant P. aeruginosa infections.

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