A High-Throughput In Vitro Model Illustrating Potential Microbiological Interactions During Treatment of Pseudomonas Aeruginosa Biofilm Associated Infections

Walid El-Khatib, Virginia Haynes, and Ayman Noreddin
University of Minnesota, Duluth

Objective: Amend a real-time, high-throughput method of bacterial growth detection for use as a model of biofilm response to co-administered pharmaceuticals during the treatment of devise associated infections. Background: Biofilms are the root etiology for chronic infections, particularly in regard to infections in patients with implanted medical devices. Calcium channel blockers (CCBs) are used for control of hypertension and angina and are commonly prescribed to elderly patients. We address potential interference of commonly prescribed CCBs with levofloxacin for treatment of Pseudomonas aeruginosa biofilms. Methods: Inoculum of $1-3\times 106$ CFU/mL in the log phase were seeded into each well of a polystyrene plate. Biofilms developed over 6 h at 37°C, was washed and medium containing various CCBs plus levofloxacin was added to the biofilm. OD measurements were obtained at 1 h intervals over 90 h at 37°C. Changes in turbidity were kinetically measured with a vertical photometer with a wide-band filter. Results: Mibefradil and diltiazem appear to be strongly antagonistic toward levofloxacin where both of them decrease antibiofilm effect of levofloxacin and they encourage the selection of resistant mutants from biofilm. Discussion: Implanted medical devices are quite common and are subjected to biofilm infections. Increasing multi-drug resistance underscores the need to conserve current antibiotics by judicious use. This necessitates consideration of evidence regarding antagonistic or synergistic activity of commonly prescribed drugs of different classes toward commonly used antibiotics. The combinations described here show vital and previously unreported effects of some CCBs when co-prescribed with levofloxacin on Pseudomonas aeruginosa biofilm.

