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## New Paradigm in treatment of biofilm-associated infections: Applications to *Pseudomonas aeruginosa* as a biofilm model organism

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**Introduction**: *Pseudomonas aeruginosa* causes several infections of burn tissue, colonizing the indwelling catheters, and it is the main cause of mortality in chronic cystic fibrosis patients. Furthermore, *P. aeruginosa* has become a major model organism in the biofilm research. This study aimed to assess *in vitro* the potential of antibiotic-drug interaction between a fluoroquinolone levofloxacin and different calcium channel blockers (CCBs) in the treatment of *P. aeruginosa* biofilm.

**Methods**: Inoculum (100  $\mu$ l/well) of log phase *P. aeruginosa* ATCC 27853 (1-3 × 10<sup>6</sup> CFU/ml) was seeded into polystyrene honeycomb plates. Biofilm developed over 12 h at 37°C, was carefully rinsed with sterile saline. The biofilm was then treated with CAMHII medium containing CCBs (diltiazem 10 mM, mibefradil 0.9 mM, nifedipine 0.6 mM, nicardipine 0.1 mM, verapamil 4.0 mM, amlodipine 0.4 mM, and bepridil 0.3 mM) alone or in combination with levofloxacin at two-fold serial dilutions (250  $\mu$ l/ well). The OD measurements were obtained at 1 h interval over 90 h at 37°C. The growth of both treated and untreated *P. aeruginosa* biofilm was kinetically monitored through the automated Bioscreen C (Growth Curves, Piscataway, NJ). MIC at 24 h and MPC at 90 h were determined in each case.

**Results**: The MIC for levofloxacin against *P. aeruginosa* biofilm was 2  $\mu$ g/ml while the MPC was 4  $\mu$ g/ml. Although levofloxacin MIC was maintained at 2  $\mu$ g/ml level with diltiazem, mibefradil and verapamil, its MPC was increased to >8  $\mu$ g/ml, >8  $\mu$ g/ml, and 8  $\mu$ g/ml in presence of these CCBs, respectively. Nifedipine and nicardipine had no effect on levofloxacin MIC and MPC. With amlodipine and bepridil, levofloxacin MIC was 1  $\mu$ g/ml and its MPCs were 4  $\mu$ g/ml & 2  $\mu$ g/ml, respectively.

**Conclusions**: CCBs have been used for treatment of hypertension and angina as relatively safe and effective drugs. This study revealed heterogeneous interactions between levofloxacin and CCBs against *P. aeruginosa* biofilm. Diltiazem, mibefradil and verapamil demonstrated antagonistic effects on levofloxacin activity while bepridil and amlodipine showed potential synergistic effects against *P. aeruginosa* biofilm.

## Biography

Walid F. Elkhatib is the Head of Microbiology and Immunology Department at Faculty of Pharmacy, Ain-Shams University, Egypt. He is currently a visiting scholar at the School of Pharmacy, Hampton University. His primary areas of research interest are biofilm associated infections and pharmacokinetic-pharmacodynamic modeling of antimicrobials. For the last seven years, Elkhatib lead many interdisciplinary collaborative research projects in multiple institutions including Ain-Shams University (ASU), Hampton University (HU), Eastern Virginia Medical School (EVMS), Christopher Newport University (CNU), William & Mary Applied Research Center (WM-ARC). Elkhatib has an ultimate goal to promote international collaborative research on infectious diseases therapies aiming to improve patients' healthcare worldwide. Elkhatib has outstanding records of scientific and academic accomplishments with multiple publications and numerous presentations in both national and international symposia and conferences. He served as a scientific reviewer for some prestigious journals as well as other national research institutions. Owing to his excellent scholarly activities in both teaching and research, he has received different awards and honors including Egyptian Partnership & Ownership award (Twice), ICAAC ID Fellows Grant Program awarded by American Society for Microbiology (ASM), Institution and Individual Award of Egypt (Single yearly award in the field of Pharmaceuticals & Biopharmaceuticals), Ain-Shams University award of outstanding publications (Five), Appreciation award from Faculty of Pharmacy, Ain-Shams University for participation in Quality Assurance Unit and accreditation, and Ain-Shams University appreciation award for outstanding scholarly activities.

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