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Antibiofilm effect of vancomycin alone and in combination with various QSIs on mono and multispecies biofilms of S.aureus

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Background: Polymicrobial biofilms are common problem in nosocomial infections. *Staphylococcus aureus,* one of the major pathogen related with the biofilm infections, is an important trouble in hospitals. Quorum sensing is an alternative strategy in fighthing biofilm infections and some natural quorum sensing inhibitors (QSI) were found successful to interfere with the infections.

Material/methods: Polymicrobial biofilms were reproducibly grown, consisting of *S. aureus, E.faecium, P. aeruginosa and C. albicans* in a 96-well microtiter plate. We determined the antibiofilm effect of vancomycin and some natural QSIs alone or in combinations on sessile cells of susceptible S.aureus and MRSA isolates respectively in both mono and multispecies biofilm model in order to gain more insight into the role of biofilm composition on efficacy of the agents. Vancomycin combinations of QSIs such as cinnamaldehyde, resveratrol, L-canavanin, 4-nitropyridine N-oxide, p-benzoquinon, farnesol, epigallocatechin gallate, catechin hydrate, curcumin, baicain hydrate ve esculin hydrate and cyclic di-GMP inhibitors such as sulfatiyazol and azathioprine were tested with MBEC assay and MBIC, MBEC and log reduction of the antimicrobials were determined.

Results: Vancomycin significantly decreased the sessile cells of *S.aureus in* mono biofilms up to 4 µg/ml and completely killed the cells above of this concentrations. Combinations of vancomycin with sulfatiyazol, 4-nitropyridine N-oxit, esculin hydrate, cinnamaldehyde and farnesol killed completely the biofilm cells even in the minimum concentration tested (0.5 µg/ml) and the combinations with curcumin, azathioprine, resvatrol, epigallocatechin and baicalein hydrat were found effective to the cells when compared with vancomycin only. Sessile cells of the *S.aureus* in polymicrobial biyofilm were found 16 times more susceptible to vancomycin compared to the cells in monomicrobial biofilms. The study also showed that combinations of QSIs with vancomycin were more effective to the S.aureus biofilm cells in polymicrobial biofilms by comparison with the monomicrobials.

Conclusions: Combinations of sulfatiyazol, 4-nitropyridine N-oxit, esculin hydrate, cinnamaldehyde and farnesol with the vancomycin kills the *S.aureus* cells completely and increase the effect of vancomycin as an antibiofilm agent. Curcumin, azathioprine, resvatrol, epigallocatechin and baicalein

hydrat have also additive effect on antibiofilm property of vancomycin. *S.aureus cells* in polymicrobial biyofilm were more susceptible to vancomycin and vancomycin combinations of QSIs when compared with the cells in monomicrobial biofilm.