

# Novel Combination Treatment of Protease, DNase I, and Antibiotic for Biofilm-Involved *Staphylococcus epidermidis* Infections

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Biofilms play a key role in bacterial resistance against antibiotics. Formation of biofilms enables *S. epidermidis* to colonize indwelling medical devices and become a major cause of nosocomial infections. 50% of clinically isolated *S. epidermidis* from inpatients are biofilm-forming and 95% are methicillin-resistant. Formation of biofilms and antibiotic-resistant strains render *S. epidermidis* infections a serious health issue- single antibiotic treatment often fails and removal of the infected catheter or prostheses is required. The development of more effective methods to treat biofilm-involved *S. epidermidis* infections will be a major step forward to counter such infections. To simulate *S. epidermidis* biofilm-involved infections, the two chosen clinical isolates represented the most prevalent strains: biofilm-forming and methicillin-resistant. This study confirmed the significant presence of eProteins and eDNA in *S. epidermidis* biofilms and found that the most effective biofilm degradation (52.5%) is achieved by the dual degradation method of protease K 1U/ml, 2hours, and DNase 20ug/ml, 12 hours. Pre-treating biofilm with this method enhances the bactericidal efficacy of Vancomycin and Linezolid by over 90% ( $P < 0.001$ ). This study proved the effectiveness of the novel Protease + DNase + antibiotic combination treatment for treating biofilm-involved infections by reducing biofilm biomass and enhancing the bactericidal effect of antibiotics.