Improving Efficacy of Photodynamic Therapy for Bacterial Biofilms Using Different Nanosystems

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ABSTRACT

Biofilms are involved in approximately 80% of human infections. The efficiency of photodynamic therapy (PDT) as a new technique to treat biofilms can be enhanced by various nanotechnology platforms.

Here we aimed to improve the efficacy of PDT for bacterial biofilms using different nanosystems (nano-photosensitizers).

The photosensitizer systems were synthesized and characterized by several techniques. At first, in vitro phototoxic effect of the nano-photosensitizers on 24 h-old biofilms of Staphylococcus aureus and Pseudomonas aeruginosa was studied. Also, in vitro cytotoxicity and phototoxicity of these photosensitizer systems (under the same experimental conditions as used for the antibiofilm photodynamic therapy) was assessed on human dermal fibroblasts. In the next step, in vitro phototoxic effect of the best photosensitizer system (considering efficiency and safety) on biofilms of different ages (24, 48, 72 and 96 h) was studied. Finally, to determine the effect of the two best photosensitizers-PDT on P. aeruginosa biofilm structure, three-dimensional (3D) morphology and surface of biofilm was investigated by atomic force microscopy (AFM).

PDT mediated by methylene blue-based photosensitizer systems including methylene blue+chitosan nanoparticle (mixed), methylene blue-chitosan nanoparticle (encapsulated), methylene blue-gold nanoparticle (conjugated) and methylene blue-graphene oxide quantum dot (conjugated) resulted in increased antibiofilm efficiency than MB-mediated PDT alone. Also, the studied nanoparticle-based photosensitizer systems including g-C3N4 nanoparticle and Ag/SiO2 co-doped fullerene showed significant antibiofilm PDT. At the same experimental conditions, <30% of the fibroblasts were photoinactivated. Methylene blue-conjugated gold nanoparticles (as the best photosensitizer system)

exhibited significant antibiofilm PDT efficacy against mature biofilms.

An analysis of the AFM topography 3D-images showed that PDT mediated by Ag/SiO2 co-doped fullerene and methylene blue-graphene oxide quantum dot induced severe morphological and surface alterations (loss of the typical cell morphology and increase in surface roughness, respectively) of P. aeruginosa biofilm.

The present findings showed that nanoparticles can enhance the efficacy of antibiofilm PDT through various processes (such as drug delivery, surface plasmone resonance effect, fluorescence quenching and antimicrobial/antibiofilm activity).

PDT mediated by methylene blue-conjugated gold nanoparticles, Ag/SiO2 co-doped fullerene or methylene blue-graphene oxide quantum dot offer a new modality for fast and efficient destruction of biofilms, suggesting their potential use in chronic wound healing.

Keywords: Photodynamic Therapy, Nanotechnology, Biofilm, Wound