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Evaluation of the antibacterial activity of gallic acid anchored phthalocyanine-doped silica nanoparticles towards *Escherichia coli* and *Staphylococcus aureus* biofilms and planktonic cells

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ABSTRACT

In this work, we have described the synthesis of phthalocyanine complexes Zn(II) *tetrakis* 4-(5-formylpyridin-2-yl)oxy) phthalocyanine (**2**), Zn(II) *tetrakis*-1-butyl-4-(2-(6- (*tetra*-phenoxy)pyridin-3-yl) vinyl)pyridin-1-ium phthalocyanine (**3**) and Zn(II) *tetrakis* 1-butyl-5-(2-(1-butylpyridin-1-ium-4-yl)vinyl)-2-(*tetra*-phenoxy)pyridin-1-ium phthalocyanine (**4**). The effect of a varying number of charges when the Pc complexes are alone or grafted in gallic acid (GA) tagged silica nanoparticles on photodynamic antimicrobial chemotherapy (PACT) is investigated toward *Staphylococcus aureus* (*S.aureus*) and *Escherichia coli* (*E.coli*) in both planktonic and biofilm forms. Complex **4**, bearing a total of 8 cationic charges, displayed the highest activity with log CFU (colony forming units) values of 8.60 and 6.42 against *E.coli* and *S.aureus* biofilms, respectively. The surface stability of *E.coli* and *S.aureus* biofilms in the presence of **4** and its conjugate was analyzed using cyclic voltammetry. Scanning electron microscopy (SEM) and Raman spectra are also used to study the conformational and biochemical changes within biofilm upon subjecting them to PACT.

1. Introduction

Infections caused by drug and multidrug-resistant bacteria are of great concern [1–3]. *S. aureus* and *E. coli* are amongst the most frequently encountered bacteria in hospitals [2]. Bacteria tend to attach to solid biotic or abiotic surfaces where they form biofilms [4,5]. Bacterial biofilms are composed of bacteria aggregates enclosed in an matrix containing proteins, polysaccharides, and DNA [6]. This structure provides an excellent defense mechanism against immune response and blocks antibiotic penetration [5,7]. The inefficiency of existing therapies in clinical use has led to intensive research for developing novel therapeutic strategies aimed at enhancing eradication of bacterial biofilms.

Photodynamic antimicrobial chemotherapy (PACT) has received considerable attention for eradication of drug resistance microorganisms. PACT combines light, oxygen and a photosensitizer (PS) to generate reactive oxygen species (ROS). In PACT, microbes are eliminated by nonspecific oxidative damage by ROS, such as singlet oxygen and hydroxyl radicals which are also involved in photodynamic therapy of cancer [8–12]. Phthalocyanines (Pcs) will be used as PSs in this work. Pcs are a group of synthetic pigments made of four isoindole units linked together to form a macrocyclic ring with properties suitable for applications in PACT, such as efficient singlet oxygen generation, high photo-toxicity, and high thermal and light stability [13,14]. The Pcs synthesized in this work bear a bulky cationic substituent that suppresses aggregation, which is known to hinder the reactivity of the Pc [15]. In our previous studies, we successfully illustrated the PACT activity of cationic styryl pyridine triphenyl phosphonium (TPP+)-based Pcs against *E. coli* [16]. Cationic Pcs are known to be more effective than neutral and anionic Pcs against Gram (−) bacteria [17,18] such as *E. coli*, which is employed in this work. The cationic Pcs in this work are embedded in mesoporous silica nanoparticles (SiNPs). Encapsulation of Pcs into SiNPs can prevent or reduce aggregation and can also protect the loaded Pc molecules from degradation [19,20]. Mesoporous SiNPs contain a complex 'worm-like' network of channels throughout the interior, so they have large surface areas and extraordinarily high drug-loading capacity. We have reported on the PACT activity of Pcs when embedded in SiNPs [21]. The Pcs reported contained four charges, in the work the number of charges is increased. An increase in the number of positive charges has been reported to improve PACT activity [16]. To go a step further in improving the PACT activity against *S. aureus* and *E. coli,* the MPc-SiNPs are linked with gallic acid (GA). GA is a hydroxybenzoic acid extracted from plants and is reported to possess

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