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Detonation nanodiamonds-phthalocyanine photosensitizers with enhanced photophysicochemical properties and effective photoantibacterial activity

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ABSTRACT

The nanophotosensitizers based on acetophenoxy tetrasubstituted metallophthalocyanines (MPc) and detonation nanodiamonds (DNDs) were successfully formed and their photophysicochemical properties were determined. The zinc(II)Pc and indium(III)Pc complexes along with their nanoconjugates were found to have high singlet oxygen quantum yields (0.72 – 0.84) associated with the heavy central metal effect. The ability of the functional groups present on the DNDs to bind to the bacteria cell and the improved solubility of the nanoconjugates due to DNDs resulted in effective photodynamic antimicrobial therapy (PACT) activity against *S. aureus* planktonic cells, with the highest log reduction of 9.72 ± 0.03 for the conjugate of InPc conjugate with DNDs after 30 min irradiation. PACT studies were investigated at a dose of 10 μg/mL for each sample. The results suggest that the readily synthesized nanoconjugates can be used as appropriate PACT agents.

1. Introduction

Light-harvesting compounds such as metallophthalocyanine (MPc) complexes have captivated great attention as the best candidates in various biomedical areas including photodynamic therapy (PDT), photodynamic antimicrobial therapy (PACT), etc. [1–5] owing to their outstanding properties such as intense absorption in the near-IR region, capability to produce high singlet oxygen, and low toxicity in the dark [6].

Photodynamic antimicrobial chemotherapy has been discovered as a non-invasive optional technique to address drug resistance by pathogens [1–5,7–10]. The photodynamic ablation process of bacteria through PACT involves the interaction between a nontoxic photosensitizer such as MPc or derivatives, and a visible light in the presence of molecular oxygen which exists in the bacterial tissues. This interaction results in the generation of reactive oxygen species (ROS) such singlet oxygen and free radicals that irreversibly lead to the apoptosis and bacteria cell deaths [11–15].

Hence, it is critically important to design new types of photosensitizer systems that exhibit enhanced photoinhibition potency leading to successful and complete bacteria death. A number of nanosystems have been employed in the biomedical fields [16–18]. Nanomaterials (nanoparticles in particular) improve the photoactivity of photosensitizers [19]. In the present work the nanoparticles of interest are the detonation nanodiamonds (DNDs). DNDs have also been used in many applications including drug delivery and antibacterial activity [20–23]. We report on the non-covalent conjugation of DNDs to the synthesized acetophenone tetrasubstituted MPcs, hence forming systems that display all the advantages of two unique groups (DNDs and phthalocyanines) on a single entity that might become promising photoantimicrobial agent. The combination of these two groups to form a single nano-moiety might result in enhancing both therapeutic activity and the diagnostic behavior of the target compounds.

Similar to other carbon materials, DNDs antimicrobial activity is likely linked to the reactive oxygen-containing groups on their surfaces. DNDs have core-shell structural design with diamond inner core (sp^3 carbon atoms) and graphitic outer shell (sp^2 carbon atoms) with hanging bonds ended with functional groups, which include carboxylic acid groups, anhydride, hydroxyl groups and epoxide groups. Due to the presence of carboxylic groups, DNDs suspensions are stable in water and have the capability of complexing with water soluble drugs [24], which is an advantage over other carbon nanomaterials. The presence of carbonyl groups in graphitic carbon nitride has been reported to remarkably increase singlet oxygen ($^1O_2$) production and suppress the generation of other reactive oxygen species (ROS) [25,26].

We recently reported on the synthesis of acetophenone tetrasubstituted phthalocyanines, [2,9(10), 16(17), 23(24)-tetrakis-(4-acetophenoxy) phthalocyaninato (TAPPc, **1**); 2,9(10), 16(17), 23(24)-tetrakis-(4-

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