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Effect of number of positive charges on the photophysical and photodynamic therapy activities of quarternary benzothiazole substituted zinc phthalocyanine

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ABSTRACT

The synthesis, photophysicochemical and photodynamic therapy (PDT) activity of quaternary benzothiazole substituted zinc phthalocyanine (**2**, containing two charges, and **3**, containing four charges) are reported in this work. Furthermore, the activity of the synthesized complex was compared to non-quaternary derivative (**1**). Higher triplet and singlet oxygen quantum yields of 0.92 and 0.85, respectively, for quaternized complexes **2** and **3** compared to complex **1** alone. Complexes **1**, **2** and **3** showed relatively no dark toxicity against the epithelial breast cancer cells with cell survival of above 90 ± 3%. The quaternary derivatives (**2** and **3**) showed superior PDT activity with 30% or less of viable cells at concentration of 50.0 μg/mL in comparison to complex **1** alone which further lay credence to the importance of quaternization in the enhancement of PDT activity.

1. Introduction

Photodynamic therapy (PDT) has been on the forefront among the emerging cancer therapy methods, owing to its non-invasive nature, fewer side effects, negligible drug resistance and low systemic toxicity [1,2]. In PDT, illumination of a photosensitizer with light of appropriate wavelength and in the presence of molecular oxygen results in the production of singlet oxygen and other reactive oxygen species (ROS) that locally kill the cancerous cells [2]. The simultaneous cancer imaging and therapy abilities of activatable photosensitizers, such as porphyrin, phthalocyanine and bacteriochlorin derivatives, have been demonstrated and some of these photosensitizers have been approved for clinical applications [3]. Research in designing ideal phthalocyanines for PDT application has been a major challenge, because preferred molecules should ideally have a favorable lipophilic-hydrophilic balance. Many and diverse solutions have been proposed to overcome the shortfalls of currently used photosensitizers, of which limited solubility and the very undesirable aggregation in commonly used solvents cause the most problems.

Since the cell membrane is negatively charged [4], photosensitizers which are negatively charged are not taken up by cells as much as the positively charged ones. Thus, studies have shown that positively charged photosensitizers have high PDT activity [5,6], hence in this work positively charged Pcs are employed. Benzothiazole substituted Zn phthalocyanines are employed in this work. The Pcs are: tetrakis [(benzo[d]thiazol-2-ylthio)phthalocyaninato] zinc(II) (**1**), di-*N*-methyl-2-tetrakis[(benzothiazoliumphenoxy) phthalocyaninato] zinc (II) iodide (**2**) and tetra-*N*-methyl-2-tetrakis[(benzothiazoliumphenoxy) phthalocyaninato] zinc (II) iodide (**3**).

The presence of benzothiazole in complex **1** allows for quaternization, hence water solubility. The quaternization using already formed Pc is a well-known method [7–9] and it was employed in this work. This method resulted in a partially quaternized Pc containing two positive charges (complex **2**). Another method where by the phthalonitrile was quaternized before the formation of Pc is employed to form a fully (four charges) quaternized Pc (complex **3**).

The photosensitizing properties of benzothiazole moiety has been reported [10], hence enhancement of photosensitizing ability through synergistic effect is expected in the quarternary benzothiazole substituted phthalocyanine employed in this work. Quarternization of the Pc is expected to improve water solubility and reduce aggregation in water.

2. Experimental

2.1. Materials

Methyl iodide, zinc acetate, 1, 8-diazabicyclo [5.4.0] undec-7-ene

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