



Photophysical and photodynamic therapy activity of highly water-soluble Zn(II) phthalocyanines

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ABSTRACT

The syntheses of two zinc(II) phthalocyanines (ZnPcs) having either imidazole (ZnPc 1) or pyridiloxy (ZnPc 2) moieties as their macrocycle substituents are reported. Quaternization of the ZnPcs with methyl iodide afforded water soluble cationic phthalocyanines. The photophysical, photochemical properties and photodynamic therapy (PDT) activity of the ZnPcs were studied in solution. The fluorescence quantum yield and lifetime of ZnPc 1 were higher as compared to ZnPc 2. ZnPc 2 afforded higher triplet state (Φ_T) and singlet oxygen quantum yields (Φ_Δ) in comparison to ZnPc 1. The PDT activity of ZnPcs was investigated against human breast adenocarcinoma cells (MCF-7). The two compounds afforded a very minimal *in vitro* dark cytotoxicity with 85% viable cells at concentration $\leq 80 \mu\text{M}$. On irradiation of the cells having the ZnPcs, $\geq 50\%$ cell death was recorded for ZnPc 1 which was also evidenced by the cells photo-micrograph.

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1. Introduction

Photodynamic therapy (PDT) is a therapeutic method that has attracted much attention due to its high selectivity towards tumour cells, low-cost and reproducibility making it a favorable alternative or adjuvant to traditional cancer therapies such as chemotherapy and radiotherapy [1]. A vital component of PDT is the photosensitizer (PS) which absorbs light of a specific wavelength leading to the formation of excited triplet state PS which subsequently transfer its energy to ground state molecular oxygen producing the reactive oxygen species known to be the dominant agent responsible for selective destruction of tumour cells [2,3].

A diverse range of PS has been used as drug candidates for PDT but phthalocyanines (Pcs) were found to afford fascinating efficacy as compared to others. This is due to their low dark toxicity, high triplet state and singlet oxygen quantum yields, a strong absorption and high extinction coefficients within the therapeutic window (600–800 nm). In recent time, remarkable progress has been made in the use of Pcs as photosensitizers for PDT, which is evidenced by their successful clinical

trials [4]. However, a few limitations such as aggregation and poor amphiphilicity are known to limit their extensive biological applications [4].

The introduction of suitable amphiphilic substituents either in peripheral or non-peripheral position of the macrocycles allows for the modulation of their electronic properties and increases their solubility in most organic or aqueous media [5].

On the other hand, it is known that near infrared (NIR) light can penetrate into deeper tissues with less damage than shorter wavelength light making NIR absorbing PS attractive drug candidates for PDT. Not many organic PS fulfill this requirement and the preparation of stable NIR PS remains a great challenge [6,7].

In this context, two water soluble ZnPcs (Fig. 1) bearing either imidazolium (ZnPc 1) or pyridinium (ZnPc 2) moieties at the macrocycles peripheral positions were synthesized. The photophysical and photochemical behaviors as well as PDT activity of the compounds were investigated. Since water solubility is important for bioavailability of the sensitizer, pyridyloxy and imidazole units were chosen in order to allow for quaternization of the substituents with methyl iodide affording water-soluble cationic phthalocyanines.

It is known that functionalization at the α positions of the Pc by electron donating groups allows for decrease in the HOMO-LUMO band gap by destabilizing the HOMO orbitals and often leads to dramatic red shift in the absorption spectra when compared to similar β -substituted complexes [8,9]. In this regard, with the aim of increasing the solubility and

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