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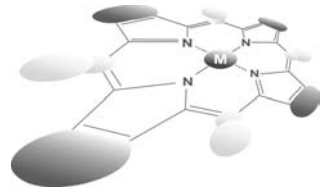

Water-soluble phthalocyanines mediated photodynamic effect on mesothelioma cells

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ABSTRACT: The new peripherally 2-mercaptopyridine tetrasubstituted zinc phthalocyanine (**2**) and its quaternized derivative (**3**) have been synthesized and characterized by elemental analysis, IR, ^{1}H NMR spectroscopy, electronic spectroscopy and mass spectra. The quaternized compound (**3**) shows excellent solubility in water, which makes it a potential photosensitizer for use in photodynamic therapy (PDT) of cancer. Fluorescence and singlet oxygen quantum yield measurements were conducted on 2-mercaptopyridine appended zinc phthalocyanines in dimethylsulphoxide (DMSO) for both the non-ionic (**2**) and quaternized (**3**) derivatives, and in aqueous media for the water-soluble complex **3**. General trends are described for fluorescence and singlet oxygen quantum yields of these compounds. In this study, the cells were incubated with a novel water-soluble zinc phthalocyanine derivative (**3**) and thereafter the cells were illuminated using broad-band incoherent light source of various energy levels. Cytotoxicity of PDT on two pleural malign mesothelioma cell lines was determined by colorimetric proliferation assay. In addition, after PDT treatment, determination of activity matrix metalloproteinases (MMPs) were evaluated using gelatine zymography.

KEYWORDS: water-soluble zinc phthalocyanines, quaternization, fluorescence, cytotoxicity, mesothelioma cell lines, matrix metalloproteinases.

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INTRODUCTION

Phthalocyanines and metallophthalocyanines have been studied extensively for many years, mostly for their use as dyes and catalysts [1, 2]. Recently, they have also found applications in many fields in materials science [3, 4], especially in nonlinear optical (NLO) devices [5], liquid crystals [6, 7], Langmuir-Blodgett films [8], electrochromic devices [9], gas sensors [10, 11], and photosensitizers [12–15], among others.

Metallophthalocyanine complexes have proved to be highly promising as photosensitizers for photodynamic therapy (PDT), due to their intense absorption in the red region of the electromagnetic radiation. High triplet state quantum yields and long triplet lifetimes are required for efficient sensitization. Phthalocyanines display cytotoxic effects when activated by light. Upon irradiation, these photosensitizers are promoted to their excited states and generate singlet oxygen. Surrounding biomolecules are damaged and this starts a series of biological responses leading to the tumor death. The photophysical properties of the phthalocyanine dyes are strongly influenced by the presence and nature of the central metal ion. Complexation of phthalocyanine with transition metals gives dyes with short triplet lifetimes (τ_T) of the photoexcited triplet state of metallophthalocyanine. Closed shell, diamagnetic ions, such as Zn^{2+}, Al^{3+} and Si^{4+}, give phthalocyanine complexes with both high triplet yields and long lifetimes [16].

PDT is an attractive new approach to treating superficially growing tumors and has been investigated under

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