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Photophysical properties and photodynamic therapy effect of zinc phthalocyanine-spermine-single walled carbon nanotube conjugate on MCF-7 breast cancer cell line

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ABSTRACT

The present study shows improved photodynamic therapy (PDT) effect of zinc mono carboxy phenoxy phthalocyanine (ZnMCPPc (**1**)) upon conjugation to spermine (via amide bond) as a targeting molecule on MCF-7 breast cancer cells. The ZnMCPPc-spermine (**2**) conjugate was adsorbed onto single walled carbon nanotubes (represented as ZnMCPPc-spermine-SWCNT (**3**)). There was no change in the fluorescence quantum yield of complex **1** following formation of **2** or **3**. Complexes **2** and **3** showed improved photophysical properties; with over 50% increases in triplet and singlet oxygen quantum yields compared to **1**. Complexes **1**, **2** and **3** were relatively not toxic to MCF-7 cancer cells when incubated with 5–40 μM of each complex for 24 h in the dark. The PDT results showed that at 40 μM complex **1** resulted in only 64% decrease in cell viability, while **2** and **3** improved the PDT effect of **1** to 97% and 95% decrease in cell viability at 40 μM respectively.

1. Introduction

Photodynamic therapy (PDT) is a minimally invasive treatment modality of tumor cells. PDT requires light, a photosensitizer and molecular oxygen. Following administration of a photosensitizer topically or intravenously to cancerous cells, the photosensitizer is activated by light of specific wavelength (tuned to the maximum absorption wavelength of the photosensitizer). The electronically excited photosensitizer transfers energy to ground state molecular oxygen to produce excited singlet oxygen, which is cytotoxic and thus, resulting in irreversible photo-damage of the tumor cells [1,2].

The excellent photophysical properties of metallophthalocyanines (MPcs), make them ideal photosensitizers for PDT. Depending on the central metal and the ring substituents, MPcs exhibit high singlet oxygen and triplet quantum yields, and long triplet state lifetimes. MPcs also absorb light in the red region of the electromagnetic spectrum, where the body tissue is fairly transparent [3–10]. Different MPc complexes are in different stages of clinical trials for PDT [2,11]. When treating cancer, cytotoxic agents are intended to exert their effect on rapidly proliferating cancer cells. However, cancer therapeutics lacks specificity which often results in undesirable side effects. One of the ways to improve the specificity of MPc to target cells is to link them to compounds that could help their uptake. The MPc used in this report was linked to spermine and the MPc-spermine conjugate was tested *in vitro* on MCF-7 breast cancer cells. We report for the first time the synthesis, photophysical properties and PDT effects of zinc mono carboxy phenoxy phthalocyanine conjugated to spermine (represented as ZnMCPPc-spermine (**2**)) on MCF-7 cancer cells. Spermines are found in nature and have been shown to have a variety of biological importance [12–15]. Spermine is an example of polyamines, which are essential for cell growth due to their ability to bind strongly to deoxyribonucleic acid (DNA) resulting in replication and transcription of cells, among other functions [16]. Rapidly proliferating tumor cells contain high concentrations of polyamine [17]. There are reports on improved PDT activity of porphyrin in the presence of spermine [18]. Lamarche et al. [18] reported on the PDT activity of porphyrin-spermine conjugate against K562 human chronic myelogenous leukemia cells. Low PDT activity of different porphyrin in the presence of polyamine on human glioma T98G cells was however reported by Bhupathiraju and Vicente [19]. Porphyrins have low absorption in the visible region where cells are transparent, while

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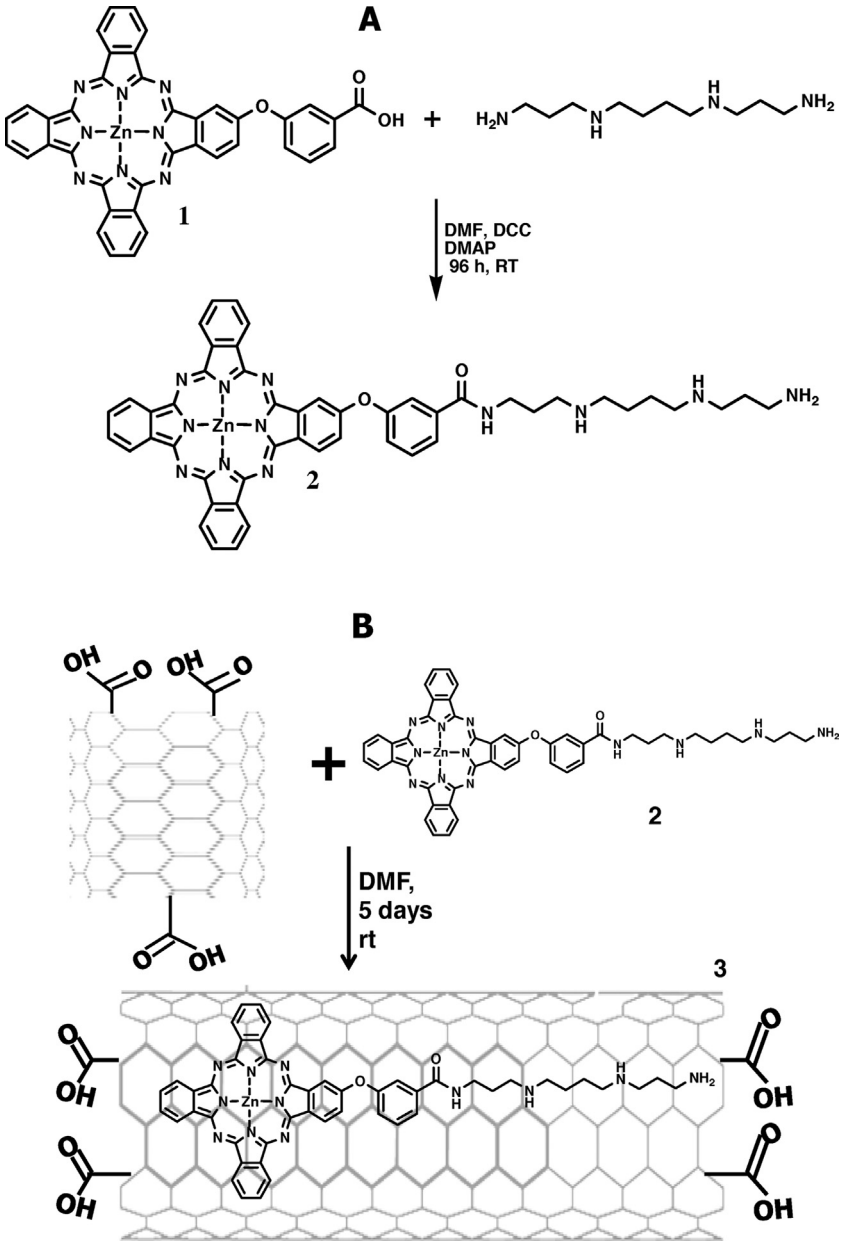
Pcs absorb strongly in this region. MPc-spermine complex reported in this work exhibited very high singlet oxygen quantum yield, resulting in improved PDT efficiency on MCF-7 cells.

Single walled carbon nanotubes (SWCNTs) have emerged as both anticancer drugs and drug delivery agents [20–23]. SWCNTs have strong optical absorption in the near infrared region, which extends to the UV region, hence can kill cancer cells through photothermal effect (PTT). Their hollow-like interior makes them an effective transport agent for other drugs including photosensitizers, into cancerous cell [23]. ZnMCPPc-spermine (**2**, Scheme 1) conjugate was immobilized onto SWCNTs (represented as ZnMCPPc-spermine-SWCNT (**3**)) and tested on MCF-7 cancer cells. There have been reports where SWCNTs were used as drug delivery agents and as anticancer drugs on MCF-7 cancer cells [24–26]. Herein, we are investigating for the first time the effect of SWCNTs on the photophysical properties of ZnMCPPc-spermine conjugate and on their PDT activity on MCF-7 cancer cells.

2. Experimental

2.1. Materials

Single-walled carbon nanotubes (SWCNT-COOH, 1–5 nm in diameter and 1–5 μm in length) were obtained from Nanolab. Dimethylsulphoxide (DMSO), dichloromethane (DCM), methanol, dimethylformamide (DMF), methanol and tetrahydrofuran (THF) were obtained from SAARCHEM. MCF-7 breast cancer cells were obtained from Cellonex®. Dulbecco's phosphate-buffered saline (DPBS) and Dulbecco's modified Eagle's medium (DMEM) were obtained from Lonza®, 10% (v/v) heat-inactivated fetal calf serum (FCS), 100 μg/mL-penicillin–100 unit/mL-streptomycin–



Scheme 1. Synthetic routes for ZnMCPPc-spermine-SWCNT (**2**) (A) and ZnMCPPc-spermine-SWCNT (**3**) (B).