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Photophysicochemical and photodynamic therapy properties of metallophthalocyanines linked to gold speckled silica nanoparticles

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ABSTRACT

This work reports on the linkage of 2(3),9(10),16(17),23(24)-tetrakis [(benzo[*d*]thiazol-2-yl phenoxy) phthalocyaninato] zinc(II) (**1**) and indium(III) chloride (**2**) to gold speckled silica (GSS) nanoparticles *via* gold to sulphur (Au-S) and gold to nitrogen (Au-N) self-assembly to form the conjugates: **1**-GSS and **2**-GSS. The formed conjugates were characterized using microscopic and spectroscopic techniques, and the photophysicochemical properties and photodynamic therapy (PDT) activity against human breast adenocarcinoma cell line (MCF-7 cells) were studied. The conjugates afforded decrease in fluorescence quantum yields with corresponding increase in triplet and singlet oxygen quantum yields when compared to phthalocyanines alone. Singlet oxygen is cytotoxic to cancer cells hence it is important for PDT. The *in vitro* dark toxicity of complex **2** and **2**-GSS against MCF–7 cells showed ≥93% viable cells within concentration ranges of 10–160 μg/mL. **2**–GSS showed enhanced PDT activity with less than 50% viable cells at 80 μg/mL as compared to **2** and GSS alone which showed > 60% viable cells within 10–160 μg/mL. The observed improvements in the PDT activity of **2**-GSS could be attributed to the high singlet oxygen generation of **2**-GSS compared to **2** alone in addition to the phototoxicity of GSS.

1. Introduction

Phthalocyanines (Pcs) are aromatic macrocyclic compounds composed of four isoindole units linked by nitrogen atoms [1,2]. The macrocycle can accommodate most metal ions in the central cavity, hence a range of different metal/metalloid phthalocyanines (MPcs) have been synthesized [1,3]. Depending on the central metal, MPcs are characterised by high triplet state and singlet oxygen quantum yields, and long triplet lifetimes, making them ideal candidates as photosensitizers (PS) for photodynamic therapy (PDT) [4–6]. Pcs with diamagnetic metals such as Zn^{2+}, Al^{3+}, Ga^{3+} and In^{3+} have shown great potential as PDT agents [4,7–9].

Pcs are capable of absorbing visible light, which excites them to an excited singlet state, consequently populating the excited triplet state through the intersystem crossing. Subsequently the excited triplet state transfers its energy to the ground state molecular oxygen generating a reactive oxygen species that destroys tumour cells [10]. The presence of heavy atoms in the central cavity of these Pcs gives rise to improved triplet quantum yields through spin orbit coupling (also known as heavy atom effect) which promotes intersystem crossing of the PS from the singlet excited state to the triplet state [11–13]. High triplet and singlet oxygen quantum yields are important for PDT as explained before. However, poor selectivity of MPcs towards cancer cells is still a major challenge in the application of these PSs for PDT hence they are now linked to nanocarriers for improved targeting through enhanced permeability and retention (EPR) effect [14–16].

Nanoparticles have shown potential as drug carriers for the intracellular delivery of therapeutics [14]. Gold and silica nanoparticles have attracted attention in biomedical applications, due to their excellent biocompatibility, and ease of surface modification [17–20]. The presence of gold in the nanocarrier is expected to improve the triplet quantum yield through the heavy atom effect of gold. Additionally, gold nanoparticles upon irradiation generate heat and have been used for photothermal therapy (PTT) [21,22]. The combination of silica and gold in gold speckled silica (GSS) nanoparticles has demonstrated high thermal stability and good PTT activity *in vitro* using the lung cancer cell line (A549) [23]. The localized rise in the temperature of GSS particles is thought to lead to the rapid injury and death of the cells [23,24]. Hence the combination of GSS with Pcs is expected to improve the singlet oxygen generation and PDT activity of Pcs.

In this work, we report on the linkage of GSS nanoparticles to 2(3),9(10),16(17),23(24) tetrakis[(benzo[*d*]thiazol-2-yl phenoxy) phthalocyaninato] zinc(II) (complex **1**) and 2(3),9(10),16(17),23(24) tetrakis [(benzo[*d*]thiazol-2-yl phenoxy) phthalocyaninato] indium(III)

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