Inorganica Chimica Acta 488 (2019) 304–311

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica

Research paper

The photo-physicochemical properties and *in vitro* photodynamic therapy activity of differently substituted-zinc (II)-phthalocyanines and graphene quantum dots conjugates on MCF7 breast cancer cell line

Lindokuhle C. Nene, Muthumuni E. Managa, David O. Oluwole, Donovan M. Mafukidze, Azole Sindelo, Tebello Nyokong*

Centre for Nanotechnology Innovation, Department of Chemistry, Rhodes University, Grahamstown 6140, South Africa

ARTICLE INFO

Keywords:
Zinc phthalocyanine
Graphene quantum dots
Singlet oxygen quantum yield
Photodynamic therapy
MCF7 cancer cells

ABSTRACT

Several differently substituted Zn(II) phthalocyanines (ZnPcs) were prepared and conjugated to GQDs. The photophysical properties were determined for both the Pcs and their respective conjugates including the fluorescence/triplet quantum yields and lifetimes as well as the singlet oxygen generating abilities. Upon conjugation to GQDs, the fluorescence of the Pcs decreased (insignificant decrease in some cases), with an increase in the triplet quantum yields. However, the singlet quantum yields of the Pcs in the conjugates did not show an increase with the increase in the triplet quantum yields, this is suspected to be due to the screening effect. The cytotoxicity of the complexes *in vitro* decreased upon conjugation, as a result of the reduced actual number of Pcs units provided in the conjugate for therapy. Upon introduction of cationic charges, the photodynamic therapy activity of the complexes increased.

1. Introduction

Conventional cancer treatment methodologies such as chemotherapy and radiation therapies have a major drawback in that they lack specificity to cancer cells [1,2]. The initiation of cytotoxicity for some of these methodologies is uncontrollable, resulting in invasiveness [3]. A relatively new methodology, photodynamic therapy (PDT), is a non-invasive and promising alternative which seeks to address these drawbacks [4]. The mechanism of action in PDT is based on the synergistic activity of light, a photoactive compound referred to as a photosensitizer, and ground state molecular oxygen to generate cytotoxic reactive oxygen species (ROS) [4,5]. Several photosensitizer compounds have been designed and studied for PDT including porphyrins, chlorins, boron dipyrromethene dyes and phthalocyanines [6–9].

Phthalocyanines (Pcs) are a group of recent generation photosensitizers which possess impressive photo-physicochemical properties which are attractive for applications such as in PDT [10–12]. Although Pcs advocate for controllable therapy in PDT, they do however, lack specificity to cancer cells [13]. For this reason, the development of delivery systems for Pcs to cancer cells is vital. Nanoparticles (NPs) have generally earned a great deal of interest in medicinal research, particularly as delivery vectors for therapeutics in oncology [14]. Several Pcs have been linked to nanoparticles such as gold [15,16] and semiconductor quantum dots for PDT [17]. However, there have been no PDT studies on the conjugates of graphene quantum dots (GQDs) and Pcs, despite the fact that GQDs are well known PDT agents [18].

GQDs are a group of fluorescent carbon-based nanomaterials which have demonstrated applicability across biological, medicinal and industrial sectors [19–21]. Structurally, GQDs appear as flat graphene sheets which usually have chemically modifiable-edges to which functionalisation with desired substituents may be achieved. GQDs have been used for delivery of several cancer drugs including the well-known doxorubicin; and some porphyrins used as photosensitizers for PDT [22,23]. GQDs have also been reported to be selective to cancer cells through the enhanced permeation retention (EPR) effect, where the drug loaded onto the GQDs is likely to target the cancer microenvironment over the non-cancerous one. This is because the pores on the endothelial cell membrane of the vascular system are relatively bigger at the tumor site, allowing easier entrance of NPs such as GQDs (which are larger than drugs alone) [23–25].

Additional advantages of using GQDs as delivery agents are their biocompatibility, simple synthesis methodologies and their ability to improve the solubility of some PS in aqueous media. The conjugates of

* Corresponding author.
E-mail address: t.nyokong@ru.ac.za (T. Nyokong).

https://doi.org/10.1016/j.ica.2019.01.012
Received 10 December 2018; Received in revised form 11 January 2019; Accepted 11 January 2019
Available online 14 January 2019
0020-1693/