



## Photodynamic therapy characteristics of phthalocyanines in the presence of boron doped detonation nanodiamonds: Effect of symmetry and charge

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### ABSTRACT

The synthesis, photophysicochemical and photodynamic therapy (PDT) activities of benzothiazole substituted zinc phthalocyanine (Pc): 1 (asymmetrically substituted and composed of no charges), 2 (asymmetrically substituted and composed of three positive charges) and 3 (symmetrically substituted and composed of four positive charges), are presented. The triplet and singlet oxygen quantum yields were highest for complex 2 showing the importance of asymmetry and charge. The complexes are covalently and non-covalently linked to B doped detonation nanodiamonds (B@DNDs) to yield nanohybrids (B@DNDs-1, B@DNDs-2, B@DNDs-3). The presence of B@DNDs, asymmetry and positive charge resulted in improved PDT with the lowest cell viability being observed for B@DNDs-2 at 5%. The cell viability ranged from 5% to 7% for the nanohybrids compared to 19–26% for Pcs alone.

### 1. Introduction

Photodynamic therapy (PDT) is a cancer therapy method that has attracted attention due to its non-invasive nature, tolerable side effects, negligible drug resistance and low systemic toxicity [1,2]. This therapy involves excitation of photosensitizer with light of appropriate wavelength in the presence of molecular oxygen resulting in the generation of singlet oxygen and other reactive oxygen species (ROS) [2]. ROS are responsible for the eradication of diseased cancer cells.

Considerable attention has been given to a variety of zero dimensional nanostructured carbon materials such as graphene quantum dots (GQDs), carbon dots (CDs), fullerenes and detonation nanodiamond (DNDs) due to their excellent chemical and physical properties [3,4]. Among these, DNDs display promising properties as candidates for biomedical use due to their small particle size (~x223C4–5 nm), reasonable production cost, purity, facile functionalization, and high biocompatibility both in vitro and in vivo and have been used as PDT agents [5,6].

The size, shape, and quality of nanodiamonds are determined by the methods used in their production [7]. The nanodiamonds employed in this work were produced through the detonation process which results in DNDs with diameters of 4–5 nm. DNDs have tetrahedral network

structures, and comprise of a diamond core ( $sp^3$ ), a middle core ( $sp^2+x$ ) and a graphitized outer layer ( $sp^2$ ). The  $sp^2$  hybridization in DNDs is associated with the carbon nature of the material, which further allows for  $\pi-\pi$  interactions with other  $\pi$  containing molecules such as metallophthalocyanines (MPcs) and this is employed in this work. Introducing heteroatoms such as nitrogen, boron and sulfur to carbon materials enhances catalytic activity [8–10]. DNDs doped with B (B@DNDs) have been previously employed in applications such as cancer therapy and electrocatalysis [8, 11,12]. The activity of boron doped nanodiamonds was attributed to the ability of boron to maintain the diamond structure following doping [8], hence in this work we employ boron doped DNDs together with phthalocyanines as photosensitizers in PDT. In their pristine state, DNDs contain several functional groups present on the surface including amine, amide, alcohol, carbonyl, and carboxyl [13, 14]. These functional groups facilitate the linking of DNDs to other molecules such as MPcs. The amide linkage was utilized to covalently couple the amino group of the Pcs: 9(10),17(18),23(24)-tris[(4-benzo[d]thiazol-2-ylphenoxy)-2-aminophenoxy] phthalocyaninato] zinc (II) (1) and the corresponding quaternary analogue 9(10),17(18),23(24)-tris-N-methyl-[(4-benzo[d]thiazol-2-iumphenoxy)-2-amino-phenoxy] phthalocyaninato] zinc (II) (2), Scheme 1, to the carboxyl group of the DNDs (but non-covalent,  $\pi-\pi$  interactions are also possible),

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