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Design, optimisation, and characterisation of two- and multi-photon absorption photosensitizers for their potential application in photodynamic therapy

ABSTRACT

Many studies have been conducted regarding photodynamic therapy (PDT). Photodynamic therapy is a tool used to non-invasively treat head, neck, and skin cancers as an alternative to more invasive chemotherapy and surgical treatments. Photodynamic therapy requires the use light, a photosensitizer, and molecular oxygen to bring forth cancer cell death. In order to further optimise this remarkable phototherapy, studies have been conducted using two-photon absorption combined photodynamic therapy. Shifting to two-photon absorption offers several advantages over conventional photodynamic therapy, such as reduced thermal photo-damage of the treated area by virtue of the lower energy of the near-infrared light. Near-infrared light also allows for deeper penetration improving the possibility of treating deeper lying tumours over conventional photodynamic therapy. Therefore, the aim of this dissertation is to present several ways in which photosensitizers can be optimised for the two-photon absorption induced PDT and other application.

The work in this thesis covers the design, synthesis, optimisation, and characterisation for improving the two-photon absorption properties of photosensitizers for prospective use in photodynamic therapy. The first part covers encapsulation of a porphyrin photosensitizer using acetylated lignin to form nanoparticles. Two-photon excited fluorescence measurements were used to determine the two-photon absorption properties of the nanoparticles in both bulk solution as well as a single separated nanoparticle. Additional techniques used are two-photon absorption microscopy and atomic force microscopy.

The second part of this work focuses on the optimisation of the well-known, second-generation, photosensitizer Foscan®. Foscan® is chemically altered and the two-photon absorption properties are determined using two-photon excited fluorescence and power

dependence measurements. Calculation of the two-photon absorption cross-section values displayed improvements upon Foscan® and show promise for the adaptation of Foscan® from conventional, one-photon photodynamic therapy to two-photon.

The third part covers the design and organic synthesis of a novel porphyrin-based photosensitizer for two-photon application. Following the optimisation of several synthetic routes and the design of novel procedures, the synthesised molecules are all characterised by standard ^{1}H-NMR and mass spectrometry. The synthesised porphyrin cores are further characterised by UV-Visible absorption and their two-photon absorption properties measured using the Z-scan technique. The calculated two-photon absorption cross-section values also display modest improvements upon well-known photosensitizers.

The final part of this thesis includes the expansion of the porphyrin macrocycle. This particular work discusses expansion using naphthalene and substitution to include heavy elements (thiophene, selenophene, and tellurophene). The two-photon absorption properties of the compounds in this section are measured using the Z-scan technique and their two-photon cross-section values calculated. These molecules demonstrate reasonable values up to 1400 nm, wavelengths not previously measured for these types of compounds.

The results from each section of this thesis display improvements upon already established photosensitizers, proving the usefulness of these design changes and provide many possibilities for the future use of these types of compounds. We hope this work will aid in optimising and modifying photosensitizers for two-photon absorption applications, particularly photodynamic therapy.