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Phototoxic Activity of New Chlorin Derivatives with Potential for Treatment against Tumor Cells

Janice Rodrigues Perussi[1], Irwin A. P. Linares[1] and **Kleber T de Oliveira[2]**
[1]Instituto de Quimica de São Carlos, Universidade de São Paulo, Brazil
[2]Departamento de Química, Universidade Federal de São Carlos, Brazil

Photodynamic therapy (PDT) is based on the induction of diseased tissue damage by the combination of three components: a photosensitizer (PS), light of adequated wavelength to the PS, and molecular oxygen leading the cells to produce reactive oxygen species (ROS) and in consequence, apoptotic or necrotic death of the tumor. In this study two new chlorins with L-type shape structure were synthesized from protoporphyrin IX dimethyl ester and 1-(3-phenylpropyl)-1H-pyrrole-2,5-dione by the Diels-Alder reaction aiming to avoid self-aggregation of the chlorins in physiological medium as well as to study the photodynamic action on HEp-2 tumor cells and Vero non-tumor cells. The chlorins CHL-Ph-A e CHL-Ph-B were characterized by ^{1}H-NMR, ^{13}C-NMR, UV-Vis and high resolution mass spectroscopy (HRMS). Their photochemical properties were determined such as quantum yield of singlet oxygen with a value around $f_0 = 0.69$ and fluorescence quantum yield ($f_f = 0.0148$) along with their photodegradation. The partition coefficient (Log P) of the CHL-Ph-A is 1.44 ± 0.06 and 1.42 ± 0.03 for the CHL-Ph-B showing an important amphiphilic character. The synthesized chlorins have a strong emission in 670 nm in DMSO ($\varepsilon = \sim 2.20 \times 10^4\ M^{-1}\ cm^{-1}$), very low photobleaching, no aggregation, and a good phototoxicity leading to cell death by an apoptotic process in tumor cells as observed by fluorescence microscopy. The IC_{50} of the chlorins in tumor cells are as low as 65 nM for HEp-2 cells and they exhibited no cytotoxicity in non-tumour cells, demonstring selectivity. The results suggest that these chlorins derivatives are potential candidates to photosensitizers for PDT of cancer.

References

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