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Porphyrin derivatives: characterization of products arising from lipid photosensitization

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The elucidation of some mechanisms present in cancer cells has stimulated development of new methodologies for the treatment of diseases such as cancer, leishmaniasis, among others. Such research resulted in advances in drug modeling, making them more specific, in addition to the promotion of new therapeutic protocols, one of which is Photodynamic Therapy (PDT). [1] PDT uses a photosensitizer (PS) in the presence of oxygen and visible light to generate reactive species capable of oxidizing biomolecules, such as lipids, responsible for maintaining the integrity and essential activities of cells. [2,3]

In this context, the present work aims to compare the photodynamic efficiency and investigate the mechanism of action of two porphyrazines (Pzs), containing 3-trifluoromethylphenyl (3-CF3Pz) or 4-fluorophenyl (4-FPz) substituents, via identification of the types of radical species generated and characterization of the products formed during photooxidation of lipid membranes.

For this, the Pzs were carried in soy phosphatidylcholine liposomes at a proportion of 1 mol% PS and were excited by different light sources in the red region depending on the experiment. The assays for the detection of reactive species were carried out with electron paramagnetic resonance spectroscopy (EPR) and the lipid photooxidation products were characterized by mass spectrometry and gas chromatography coupled to mass spectrometry (GC-MS). For the in vitro phototoxicity assays, HaCaT and A-431 cell lines were used.

The in vitro studies revealed that 3-CF3Pz presented much higher phototoxic activity (IC50 0.8 µM) against A431 (tumor lineage) when compared to 4-FPz (IC50 8.2 µM). Data obtained by EPR in aqueous media show that 3-CF3Pz has a 40% higher rate of singlet oxygen production, on the other hand, other radical species such as superoxide and hydroxyl radicals were not observed in significant quantities. Despite this, the kinetics of lipid hydroperoxidation (mono, di, tri and tetrahydroperoxides) observed by mass spectrometry was similar between both Pzs. The GC-MS results suggest the formation of fatty acids for both PSs, while lipid aldehydes are observed only for 3-CF3Pz.

As a conclusion, there is a significant difference in phototoxicity between Pzs, which may be associated with the formation of short-chain lipids, such as lipid aldehydes, during the photosensitization process.

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References

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