Photochemical and Antioxidant Properties of Phenothiazine Associated to Lipid Bilayers

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Previously, it was demonstrated that the aggregates of three phenothiazine derivates used in the treatment of schizophrenia: thioridazine (TR), trifluoperazine (TFP) and fluphenazine (FP), form stable cation radicals when photoexcited by UV irradiation. However, TR, TFP and FP do not form stable cation radical when associated to lipid bilayers and promote oxidative damage in membranes. In this study, the photochemical properties of the phenothiazine nucleous (PHT) associated to mitochondrial membranes and in a mimetic model liposome were investigated. PHT exhibits hydrophobic interaction with lipid bilayers, as showed by PHT spectral changes that accompany titrations with liposomes and mitochondrial membranes. The irradiation of PHT associated to lipid bilayers reveals that contrary to TR, TFP and FP, photoexcited PHT forms stable cation radical that absorbs light with maximal at 520 nm and is responsible for appearance of a pink color. At low PHT/PCPECL ratios (1/20), the photoexcitation of PHT generates stable cation radical that is partially converted to sulphoxide and oxidized form via reaction with molecular oxygen. At high PHT/PCPECL ratios (2/1), the formation of PHT aggregates favors the cross reaction between PHT pairs leading to drug dimerization and the appearance of a blue color. In both drug/lipid ratios, photoexcited PHT did not cause damage in the membranes and further it was able to protect the membranes against added prooxidant agents, a property observed at the excited and ground states. The photochemical and antioxidant properties were maintained in PHT associated to PEG and points potential for the use of PHT in cosmetics.

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