Ruthenium phthalocyanine complex as metal-based photosensitizer. Photochemical and photobiology studies

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In recent years several articles and books have been published on the use of phthalocyanine-based compounds in photodynamic therapy (PDT). Phthalocyanines, second generation of photosensitizers, have interesting chemical characteristics like strong absorption in the therapeutic window, production of singlet oxygen, chemical and thermal stability. Understanding the relationship between molecular structure of the photosensitizers and cellular sublocalization could help in the development of new species for treatment of tumors using PDT. In this context, we are describing the synthesis, physical-chemical, photochemical properties and biological effect of new ruthenium phthalocyanine complex, [Ru(Pc)(4-ampy)$_2$] and its use as cytotoxic agent. The synthesis for the complex [Ru(Pc)(4-ampy)$_2$] was adapted by method described by Weber et al. [1] and characterized by Uv-Visible, infrared, fluorescence spectroscopy and mass spectrometry. Photochemical assays was conducted by means singlet oxygen measurement, photodegradation and excited state lifetime. Biological studies were performed with as B16F10, HCT, MNT-1 and A549 tumor cell lines and L929 as a model of healthy cells. MTS assays were performed to evaluate the cytotoxicity of the complex in different concentrations after 24h of incubation exposed to visible light treatment against dark control groups. The laser irradiation used was setup at 660 nm with fluency of 2,5 J/cm² in a continuous wave mode. The fluorescence quantum yield was 0.011 suggesting higher intersystem crossing process via spin-orbital coupling [2,3]. Continuous light irradiation at 660 nm involves no change on the intensity of Q-band in time function, which was evaluated as a characteristic of photo-stability. The [Ru(Pc)(4-ampy)$_2$] specie shows no cytotoxicity on the dark. Under PDT protocols, light irradiation at 660 nm produced cell death. Significant decrease in the cell viability was observed after 24 hours post-irradiation. At the light dose of 2,5 J/cm², the cell viability decreased 55% for A549 cells and 45% for MNT-1 (4 µM). Even preliminaries, these results indicate that the new phthalocyanine has high photodynamic activity in tumor cells and show great potential to PDT application. Biological studies centered on the western-blotting analysis have been conducted in order to specify the cell death mechanism. Take together all the photochemical and photobiological studies the ruthenium phthalocyanine compounds maybe useful in clinical therapy as new class of metal-based drug activated by light irradiation.

[1] Weber, A.; Ertel, T. S.; Reinöhl, U.; Bertagnolli, H.; Leuze, M.; Hees, M.; Hanack, M. *Eur. J. Inorg. Chem.* (2000) 2289-22294; [2] Tekdas, D. A.; Durmus, M.; Yanik, H.; Ahsen, V.; *SpectrochimicaActa Part A* 93 (2010) 313-320; [3] Guo, J-J.; Wang, S-R.; Li, X-G.; Yuan, M-Y..*Dyes and Pigments* 93 (2012) 1463-1470.

Acknowledgments: CNPq, CAPES and FAPESP (2013/08851-0) for financial support