XXVI Congresso Brasileiro de Engenharia Biomédica

Armação de Búzios – RJ – Brasil

October 21st to 25th, 2018

Development of Photosensitizer for Photodynamic Therapy

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Background, Motivation and Objective.

The photodynamic therapy it's a therapeutically technique that consist in cancer treatment and other related diseases, this therapy is based on the photo oxidation of biological material, and its activity is due to reactive species of oxygen(ROs), which are generated *In situ* and provides cellular death through visible light in the presence of a oxygen photosensitizer. The most recent researches in PDT, the themes approached are consisted of the development of new drugs, drug carriage systems, schematization of the responsible mechanisms of sensibilization and cell death induce by citolocalization of these drugs, however, a limitant factor and in-depth of photosensitizer it is the formation of self aggregation due to a strong interaction between the aromatic macrocycles. When occurs the formation of self aggregated states the interaction between the π system outcomes the interaction between the solvent and the solute, reducing its solubility and changing its physiochemical proprieties, inducing a decrease of the quantic yield of fluorescence in triplet state of singlet oxygen and consequently its photosensitizer activity. However, much work has been done with the purpose to reduce its self aggregation and it was published in JOC2011, 76, 8824–8832 (dx.doi.org/10.1021/jo201568n). The purpose of this research is to synthesize and to understand new photosensitizer behavior, in comparison to the photosensitizer published in JOC and it is already working in specific organelles.

Methods.

The new compounds were sensitized by analogous procedures to those published in JOC. Which the maleimides obtained from the anidrid maleic and correspondent amine and chlorines by Diels-Alder reaction using derivates from protoporphirine IX as schematized in figure 1.

The cytological studies are being realized in Petri dish with specification of 1,8cm of diameter with cellular concentration of 10^6 cells. mL^{-1} and incubated up to 12 hours to adhesion, after the incubation time cycle the old culture of cells were removed and replaced by another one, carrying a drug concentration of 20µg. The Petri dish was set in incubation up to 3 hours to permit the drug incorporation. After the incubation time the dish with drug was removed and the range of incorporation was defined by the difference between its absorbance with one aliquot of the solution that was add to the cell.

Results.

The chlorinic photosensitizer derivate from Protoporphirine IX were obtained with analogous yields related to those published in JOC and have show photo physical proprieties favourable to PDT with elevated quantic yield related to quantic oxygen singlet above 0,7 and fluorescence quantic yield above 0,15.

Discussion and Conclusions.

The route of synthesis in this work has followed those published in JOC 2011. Besides its excellent yields of reaction, the route of synthesis permitted the possibility to have photosensitizer with strong absorption on the therapeutically range (666 nm) spectrum which occurs a strong penetration of light in biological tissue; this compounds had shown excellent quantic yields of singlet oxygen and fluorescence as well, which makes possible the realization of treatment and diagnostic. On the other hand, the chromophorous is asymmetric which permits its permeability and insertion of biodirectioners that may lead the drug to subunits of organelles in the cell, improving its photobiology and its photodynamic effects. Thus, this work is under development and the next task is to test the sub localization in cells and its photodynamic activity *in vivo*. The promissory photo physics proprieties make the photosensitizer a remarkable treatment of uncountable diseases including tumours that are present in deeper tissues.

Figures and Tables

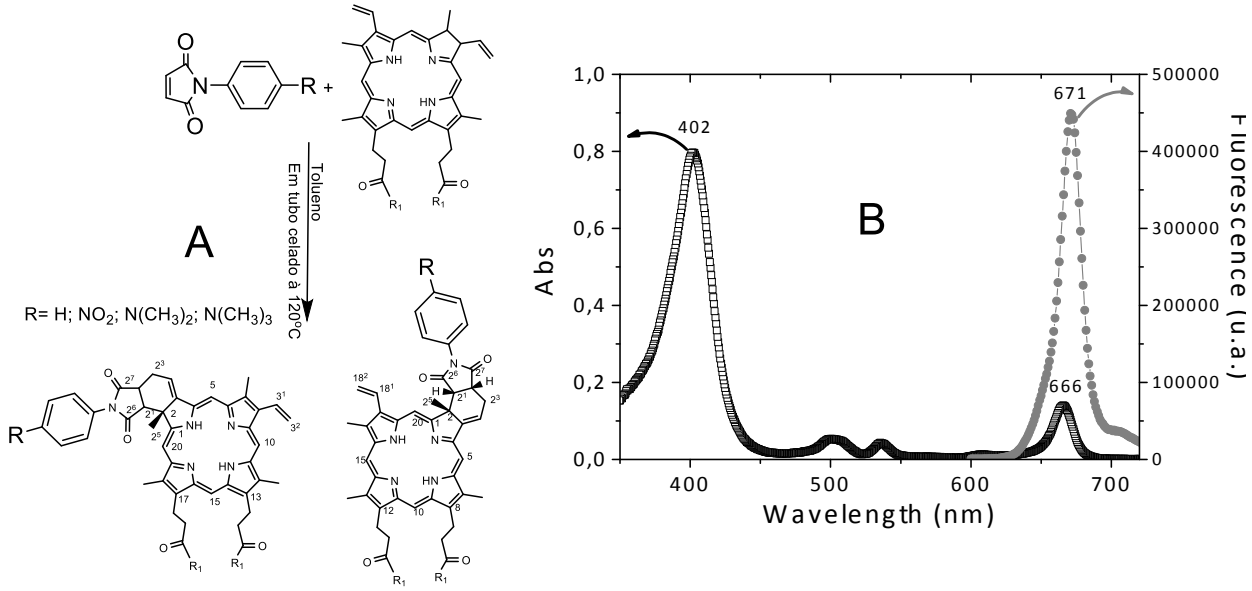

Figure 1: A) Synthetic route of new photosensitizer B) Absorption spectrum UV-Vis (left) of the new photosensitizer and fluorescence spectrum (right).

Acknowledgment. ."Center for Research on Redox Processes in Biomedicine". REDOXOME – CEPID-FAPESP (Process 2013/07937-8).

Keywords. Photodynamic therapy; Photosensitizer; Bio direction.