Effect of the Sonoluminescence on the Generation of Singlet Oxygen in Sono-Photodynamic Therapy

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Photodynamic therapy (PDT) is a minimally invasive approach for eliminating cancer cells, primarily non-melanoma, by combining light, a photosensitizing drug, and molecular oxygen to induce cell death. However, PDT has limitations due to the restricted penetration of light, hindering its effectiveness in treating non-superficial and pigmented lesions. In this scenario, sono-photodynamic therapy (SPDT) emerges as an alternative, integrating light and low-frequency ultrasound (US) with a protocol akin to PDT but with enhanced penetration capabilities.

When US propagates in a medium, small gas bubbles can be formed and begin to oscillate, a phenomenon called cavitation. If the acoustic pressure is high enough, the oscillate bubbles will implode, generating a flash of light, known as sonoluminescence (SL). This event serves as a chemical reactor and could be responsible for the generation of singlet oxygen, a reactive oxygen species (ROS) that is damaging to cells. However, there is no consensus about the exact contribution of SL in generating ROS.

This research aims to predict mathematically the amount of singlet oxygen ($^1O_2$) generated by sonoluminescence excitation and the role it plays in the generation of this reactive oxygen species under the influence of US.

In order to do that, a routine was created in the software MATLAB to calculate the number of singlet oxygen molecules generated by sonoluminescence considering different molecules of the family of phthalocyanines with the potential to be used as photo and sonosensitizeres (SS) synthesized by Karalink *et al.* (2024), Atmaca *et al.* (2023) and Atmaca *et al.* (2021). The data on the sonoluminescence spectrum was obtained from literature. The intensity absorbed by each SS was obtained from the Beer-Lambert law. From the quantum yield of singlet oxygen, known for each molecule due to light irradiation, the number of $^1O_2$ generated by SL was obtained. To verify the precision of the model, the results were compared with the data available in the literature. The results show that, for all molecules analysed, the predicted number of singlet oxygen generated is lower than the number measured in the literature, and the difference varies for each molecule. This indicates the importance of the molecule for the generation of SL and the possible presence of other phenomena in the generation of singlet oxygen.

In conclusion, the spectrum of SL should be obtained for each molecule analysed in order to achieve a more precise model. Furthermore, the SL can be responsible for the generation of singlet oxygen species in SPDT, however, other phenomena, such as pyrolysis could be more important in this process, which is fundamental for the effectiveness of SPDT treatment.

Keywords: Sono-photodynamic therapy; Sonoluminescence; Singlet oxygen production.