# Study of the Application of Fractioned Energy Dosing in Synthetic Curcumin Against Antibiotic-Resistant Bacteria

T C S Cappellini[1,2], K J S Silva[3], N M Inada[2], A R Lima[4], and V S Bagnato[2,5,6]

[1] *Department of Biotechnology, Federal University of São Carlos, São Carlos, Brazil*
[2] *Biophotonics Lab., CePOF, University of São Paulo, São Carlos Institute of Physics, São Carlos, Brazil*
[3] *School of Engineering, University of São Paulo, São Carlos, Brazil*
[4] *Laboratory of Environmental Biophotonics, University of São Paulo, São Carlos Institute of Physics, São Carlos, Brazil*
[5] *Department of Biomedical Engineering, Texas A&M University, College Station TX, USA*
[6] *Department of Biotechnology, Universidade Federal de São Carlos, São Carlos, Brazil*
Contact Email: taicruz31@gmail.com

The increasing use of antimicrobial drugs has caused the emergence of resistant bacteria in hospital environments and in the community, resulting in a global public health concern. Alternative treatments to antibiotic therapy have emerged, such as photodynamic inactivation (PDI). The PDI process is based on the use of a photosensitizer molecule (PS), which, when irradiated by a specific wavelength of light in the PS absorption range, and in the presence of molecular oxygen, forms reactive oxygen species (ROS). These are capable of causing oxidative damage to cells and, therefore, death of the target microorganism. The present study aimed to evaluate the action of synthetic curcumin as a PS, acting in the PDI process against the gram-positive bacterium Methicillin-resistant Staphylococcus aureus (MRSA), due to its known prevalence as an antibiotic-resistant pathogenic microorganism. The study was carried out with continuous (conventional) and fractional lighting. Curcumin action was evaluated at a concentration of 10 micromolar in distilled water. PS irradiation was carried out at 450 nm, provided by LED lights (BioTable®). The conventional PDI process was carried out with delivery of light doses at 5, 10 and 15 J/cm$^2$ without energy supply interruptions, while fractional PDI included 10 min intervals between equal delivered doses of 5 J/cm$^2$. The results demonstrated effective inactivation of MRSA in both treatments. Regarding conventional PDI, there was a reduction of 3.42 ± 0.23 log and 4.34 ± 0.07 log at higher doses (10 and 15 J/cm$^2$, respectively). Fractioned PDI showed 3.15 ± 0.47 log and 4.96 ± 0.58 log of MRSA inactivation for these same doses, delivered with one and two interruptions, respectively, which, despite having indicated a significant difference between them due to the known dose-dependent relationship for PDI efficiency, it was statistically similar to the respective energy doses of conventional PDI. Further research is recommended on the mechanisms involved in fractionated light delivery to elucidate possible advantages of this protocol in PDI to address the antibiotic-resistant bacteria issue, in infections and in the environment.