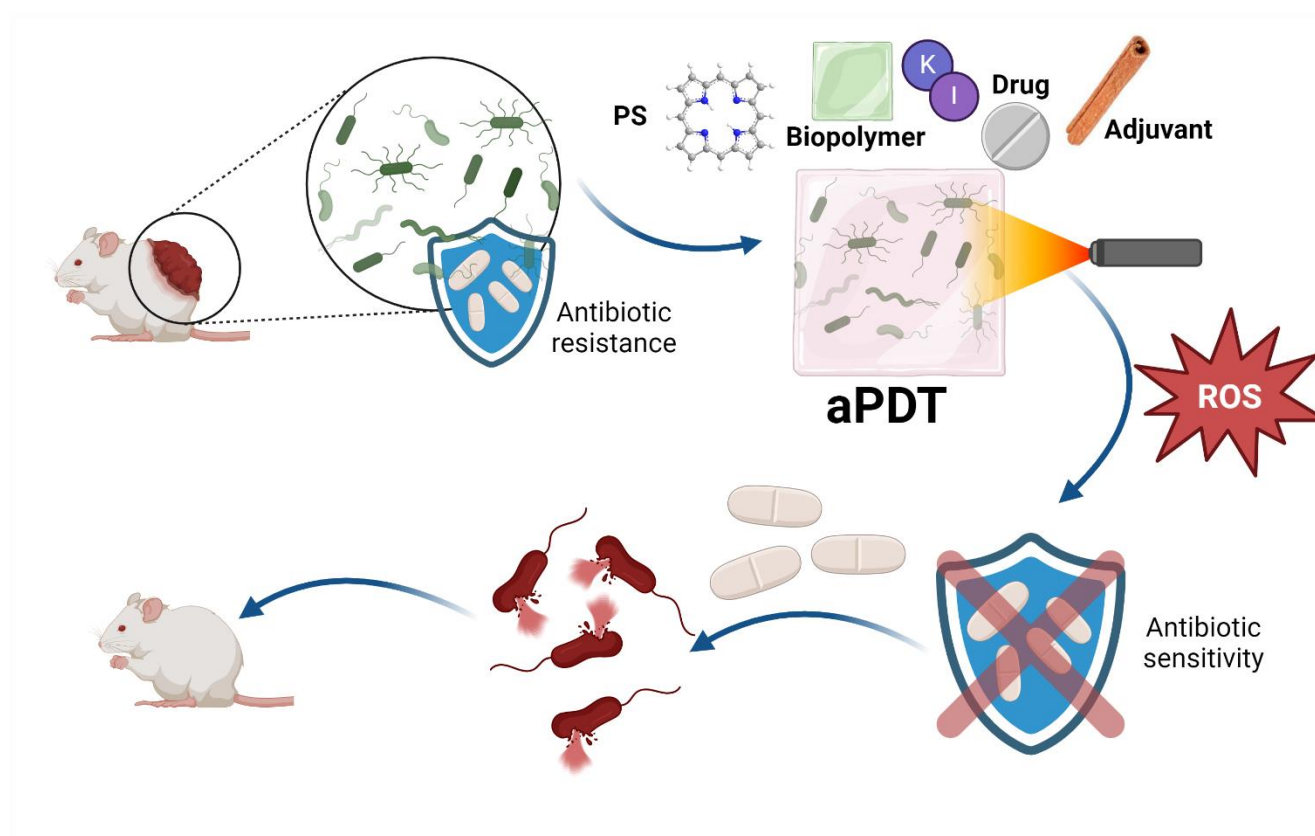


Light Against Darkness: Biocompatible Photoactivated Pharmaceuticals for Combating Multidrug Resistant Bacterial Infections in the Post-Antibiotic Era

Imagine a world where microbes are increasingly effective at ending people's lives. Sepsis, hospital-acquired infections, or wound infections are now an everyday occurrence, while at the same time antibiotics, once our main weapons, are losing their power. Bacterial multidrug resistance is robbing us of effective treatments, leading us toward darkness, where rising death rates are the price for an era of antibiotic overuse.

Our research brings a ray of light into this darkness. The project is based on Antibacterial Photodynamic Therapy (aPDT), a cutting-edge method in which light, photon-absorbing chemicals and oxygen work together to generate molecules (reactive oxygen species; ROS) capable of destroying bacteria. The chemical aspect involves synthesizing porphyrins, chlorins, and phthalocyanines with enhanced electronic absorption, optimized redox properties, and improved bacterial uptake. Functionalization strategies, including optimization of lipophilicity, molecular size, charge distribution, incorporation of various substituents/metal ions, and asymmetric influences, will be employed to enhance the efficacy of photosensitizers against both Gram-positive and Gram-negative bacteria. Their photodynamic efficacy will be tested not only on bacteria in planktonic form, but also on resistant biofilms. Advanced spectroscopic (time-resolved transient absorption spectroscopy) and microscopic techniques (FLIM, UHR-SEM, AFM, TEM, EDX) will be used to evaluate the influence of the photogenerated ROS on bacterial structure (planktonic and biofilms).



Schematic representation of Antibacterial Photodynamic Therapy against antibiotic-resistant microorganisms

The project will enable testing of photoactive formulations *in vitro* and *in vivo*, including models of wound infections and bacterial biofilms, which have so far been extremely difficult to treat. We also plan to use advanced 3D models and mouse models of wounds, including mice with diabetic infections, to confirm the efficacy of the resulting compounds under clinical-like conditions. In addition, self-cleaning surfaces will be prepared to destroy microorganisms under the influence of light, reducing the risk of nosocomial infections.

The goal of the project is to select photosensitizers in optimized formulations for effective aPDT and to develop light-activated antimicrobial surfaces. Through this research, we will try to illuminate the darkness left by antibiotics and restore effective tools in the fight against microbial multidrug resistance.