Optical signatures of molecular mechanisms in synergistic Amphotericin B systems

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Fungal infections and the ever-increasing resistance of fungi to available drugs are a significant problem in modern medicine, which is driving the search for new effective antifungal drugs for scientists in many fields. A synergistic effect between existing drugs and other bioactive compounds, including both natural and synthetic compounds, may offer an opportunity. However, the key challenge lies in understanding the molecular mechanisms responsible for this synergistic effect.

Our studies have demonstrated the potential of these new compounds to produce synergistic effects when combined with amphotericin B. This work focuses on a spectroscopic approach to analyzing synergistic mechanisms, based on the analysis of optical effects and their correlation with molecular interactions. The studies were conducted on systems containing the gold standard among antifungal antibiotics, amphotericin B. Spectroscopic analysis demonstrated that absorption spectroscopy (UV-VIS) allows for monitoring the state of antibiotic aggregation through characteristic band shifts and changes in the spectral profile. Monomer-aggregate equilibrium analysis for synergistic systems and comprehensive characterization of molecular organization changes were also conducted using other methods, including synchronous spectral measurements, time-resolved single photon counting (TCSPC), circular dichroism (CD), and dynamic light scattering (DLS) measurements. Interpretation of the obtained results was supported by quantum mechanical modeling methods (DFT and TD-DFT), which allowed us to determine how the compounds interact most favorably with AmB in solution.

The obtained results confirmed that for an effective synergistic system to form, partial deaggregation of the antibiotic is necessary. The use of such broad research methods allowed us to determine the preliminary mechanism of synergy with amphotericin B. In the future, these methods may constitute a universal tool for accelerating the search for synergistic antifungal systems or for the rational design of new synthetic compounds with promising properties.

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