Disrupting the Deadly Fungus: How Amphotericin B Targets and Destabilizes the Candida auris Membrane

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Candida auris (CA) is an emerging fungal pathogen responsible for increasing numbers of fatal infections worldwide. Currently, only a limited number of antifungal agents are effective against this microorganism, among which Amphotericin B (AmB) remains one of the most important. AmB is an amphipathic macrolide polyene antibiotic whose antifungal activity primarily involves interactions with fungal cell membrane components, particularly ergosterol. In this study, the interactions between AmB and a model membrane mimicking the lipid composition of *CA* were investigated using Langmuir monolayers as simplified biological membrane models. Thermodynamic analysis and atomic force microscope (AFM) topographical imaging were employed to characterize the molecular interactions and their effects on membrane morphology. The results demonstrated a strong affinity of AmB for the model *CA* membrane, leading to significant structural degradation and fluidization of the lipid film. Detailed analysis confirmed a particularly strong interaction between AmB and ergosterol, which occurred effectively only when the AmB molecule adopted a horizontal orientation within the monolayer. Additionally, very strong interactions were observed between AmB and phosphatidylinositol (PI), a lipid present in both fungal and mammalian membranes. These findings suggest that PI may serve as an additional molecular target of AmB, potentially contributing to its known toxicity toward mammalian cells. Overall, the study highlights the importance of both specific lipid–drug interactions and the spatial orientation of AmB molecules in determining its antifungal efficacy and selectivity.

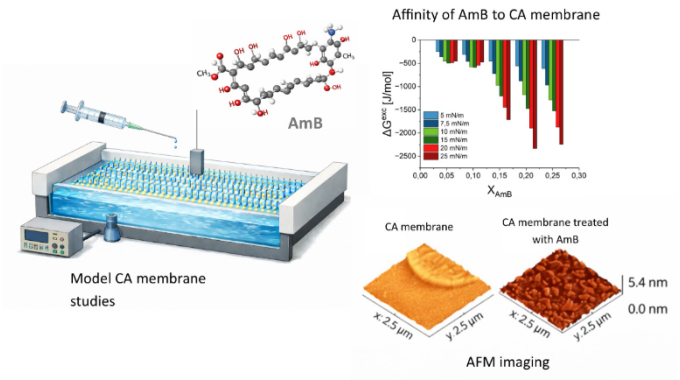

Fig. 1 Influence of AmB on Candida Auris membrane modeled with Langmuir monolayer