Summary

The doctoral thesis focuses on investigating the mechanism of action of amphotericin B (AmB), a popular antifungal antibiotic, with particular emphasis on its interactions with cell membranes. The main goal of the research was to better understand the molecular basis of AmB activity and the potential of AmB-silver hybrid nanoparticles (AmB-Ag) in enhancing antifungal efficacy. Using advanced molecular spectroscopy and imaging techniques, including time-resolved fluorescence microscopy (FLIM) and Raman spectroscopy, I analysed the interactions of AmB-Ag nanoparticles with Candida albicans fungal cells at the nanometre level. The studies showed that AmB-Ag nanoparticles exhibit exceptionally high antifungal efficacy while having low toxicity to human cells. A key finding was demonstrating that AmB penetrates lipid membranes only in the presence of ergosterol, the main sterol of fungal cell membranes. In ergosterol-containing membranes, AmB forms various molecular structures, including intramembrane clusters 20-50 nm in diameter and pores about 15 nm in diameter. The studies confirmed that AmB does not exist in membranes as a monomer, but takes on more complex forms of molecular organization in which dimers are the basic unit. The work provides new information on the molecular mechanism of action of amphotericin B, highlighting the role of cell membrane disintegration as a key factor in its antifungal activity. The use of AmB-Ag nanoparticles proved to be an effective way to increase the efficiency of antibiotic delivery to fungal cells. The results have significant implications for understanding the complex mechanisms of AmB action and may contribute to the development of more effective and safer formulations of this drug in the future, which is particularly important in the context of increasing fungal resistance to antifungal drugs.

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