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Study of self-organization of polyene antibiotic Amphotericin B methods of molecular spectroscopy

SUMMARY

Interdisciplinary research, at the border of medicinal biology and molecular biophysics was carried out, aimed to unveil - molecular mechanisms associated with various aspects of biological activity of the antifungal antibiotic amphotericin B (AmB).

Amphotericin B belongs to a group of life saving antibiotics, used to treat deep-seated mycotic infections. Despite decades of intensive research on the mode of action of AmB, exact molecular mechanisms responsible for its pharmaceutical activity and toxic side effects are not fully understood.

The main objective of the research was the unveiling and understanding of molecular mechanisms responsible for AmB toxicity, in particular, verification of the working hypothesis.

According to this hypothesis AmB spontaneously and very efficiently self-associates to dimers which further self-assemble to the tetramers. Such AmB molecular organization forms can be responsible for toxic side effects of the drug.

Research was carried out with the use of molecular spectroscopy and molecular imaging techniques applied to single model lipid membrane objects (liposomes) and single transport protein molecules ("single molecule" approach). In particular, the research was based on, Time Resolved Fluorescence, FLIM (Fluorescence Lifetime Imaging Microscopy), FCS (Fluorescence Correlation Spectroscopy), CD (Circular Dichroism) spectroscopy. Self-organization of AmB into cylindrical (pores) structures was monitored with the application of the PALS (Positron Annihilation Lifetime Spectroscopy) technique, owing to the dependence of the orthopositronium decay rate on free space dimensions in molecular structures.

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