THE INFLUENCE K^+ AND Na^+ IONS ON THE AGGREGATION OF AMPHOTERICIN B IN AQUEOUS SOLUTION AS STUDIED BY MEANS OF ELECTRONIC ABSORPTION AND FLUORESCENCE SPECTROSCOPY

M. ARCZEWSKA[1], G. CZERNEL[1], R. KOWALSKI[1], W. I. GRUSZECKI[2], M. GAGAOŚ[1]

[1]Agricultural University, Lublin;
[2]Maria Curie-Skłodowska University, Lublin

Amphotericin B (AmB) is a polyene macrolide antibiotic that is frequently applied in the treatment of systematic fungal infections. Despite its long clinical history, the molecular antifungal action of AmB is not well understood. The mechanism of AmB action is most probably directly related to the ability of the drug to form ion channels. The channels are responsible for the leakage of monovalent ions, particularly K^+, and other small molecules from the cell. The formation of these channels is highly dependent on the presence of the principial sterols (cholesterol and ergosterol) in eucaryote cell membranes. In aqueous suspensions three forms of AmB may coexist: monomers, water-soluble oligomers and non-water-soluble aggregates. The aim of this work was to study the behavior of AmB in aqueous medium as a function of pH at the presence of K^+ and Na^+ ions. The presence of net electrical charge on the amine and carboxyl groups plays an important role in the mechanism of aggregation. Titration was applied to find two values: pK_a of 2 and 10, which were assigned to carboxyl and amino group, respectively. The aggregate formation rate was dependent on the experimental conditions of the medium: its value increased at acidic pH values, while alkaline medium induced the equilibrium displacement towards the monomer formation. The molar extinction coefficient of AmB dissolved in alkaline environment indicates that water solubility of AmB was increased by addition of KOH.