DIMERS AND AGGREGATES OF ANTIBIOTIC AMPHOTERICIN B STUDIED BY FLUORESCENCE SPECTROSCOPY

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Amphotericin B (AmB) is a polyene antibiotic used in medical treatment of deep-seated systemic fungal infections. According to the general conviction, the pharmacological action of the drug is based on the formation of membrane pores that considerably affect physiological ions transport. The pharmacological effect of AmB is based on selectivity in interaction of the drug towards ergosterol versus cholesterol. Electronic absorption and fluorescence techniques were applied to investigate formation of molecular aggregates of AmB in the aqueous environment. It appears that AmB dimers, stabilized by van der Waals interactions, are present in the membrane along with the aggregates formed by a greater number of molecules. Fluorescence emission from dimeric and monomeric forms of AmB dissolved in water (pH = 5) were recorded in the spectral regions of 400–500 nm and 500 –700 nm respectively. The fluorescence excitation spectra correspond to the absorption spectra of the monomeric and dimeric forms of the drug. The large energy shift between the excitation and emission bands indicates that emission takes place from an energy level different than that one responsible for absorption. Resonance Light Scattering (RLS) was used for the study of electronically coupled chromophores, especially aggregates. It was possible to find the two lowest exciton energy levels spaced by $2\beta_1 = 5653$ cm^{-1} and $2\beta_2 = 3556$ cm^{-1} (β is a dipole-dipol coupling matrix element) by the RLS technique. The calculated distances between the centers of the transitions dipoles of the nearest neighbors in the aggregate are $R_1 = 6.1$ Å and $R_2 = 7.2$ Å. If we use these distances it is possible to calculate the size of internal diameter of the pore created, for example, with 8 molecules: $d_1 = 2.8$ Å and $d_2 = 5.4$ Å.