Fluorescence Lifetime Imaging Microscopy reveals modes of activity of the polyene antibiotic amphotericin B against biomembranes

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The polyene antibiotic amphotericin B complexed with bovine serum albumin shows an exceptionally high antifungal activity against *Candida albicans*. Fluorescence lifetime imaging microscopy analyzes show that the drug molecules complexed with the protein remain predominantly in monomeric form. The results of molecular imaging of single complex particles indicate that in most cases the antibiotic-protein stoichiometry is 1:1. The complexes can easily bind to cell membranes and enter cells, unlike amphotericin B molecules present in the aqueous phase that are effectively retained by the cell wall barrier. The results of the spectroscopic analysis suggest that the membrane bound drug molecules are oriented perpendicular to the plane of the membrane and form molecular assemblies. The complexed action of amphotericin B with the protein indicates a completely different way of incorporation into the biological membrane than drugs based on this polyene (AmBisome or Fungizone). This suggests that the antifungal activity of amphotericin B transported to cell membranes is realized via the formation of transmembrane pores that interfere with physiological ion transport. The advantages and the prospects of pharmacological use of amphotericin B complexed with protein will be discussed.

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