Mechanism of action of biolytic agents on model phospholipid-sterol systems

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The study of antifungal and antibacterial action is of great interest and there are still many unknowns concerning the action of membrane lytic materials, and the way that drugs, and other benefit agents cross the cell membrane barrier. Recently a detailed study of the mode of action of amphotericin B (AmB) was conducted by Foglia et al[1], contrasting the difference in micro-channels in models of fungal cell membranes containing ergosterol and proxys for mammalian membranes containing cholesterol. The thesis was that antifungal action was achieved through the generation of self-assembled ion channels but only where ergosterol was present in the membrane. The membrane sterols seem to play an important role in the pore formation.

Our aim as well is to carry out neutron diffraction studies to determine the molecular organisation within model membranes involving oriented bilayer stacks prepared from phospholipid:cholesterol:Agent and phospholipid:ergosterol:Agent mixtures where the Agent will be either the Membrane lytic polymer "Pp50", or other membrane lytic amphiphile agent. Both kind of agents have been shown to be membrane substantive against fungal cells whilst leaving mammalian cells intact. The levels of each Agent will be determined using the liposome rupture approach prior to beam time.
This work is part of a one-year ER project (The Framework 7 Marie Curie Initial Training Network, "Smart Nano objects for alteration of lipid bilayers") and includes as well ongoing studies involving understanding the structure of the vesicle membrane formed by such mixtures by means of SANS.