Investigation of the effect of some active principles on phospholipid-based membranes

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Phospholipid-based bilayers are widely used as model systems for studying the more complicated biological cell membranes, providing information about their structure and behavior. Here, we have been interested in investigating the effect of some active principles on phospholipid-based membranes. Such a study can help in elucidating the mechanism of action of the drugs at a molecular level, the cause of eventual toxicity when administered at high concentrations, as well as could help for a chemical design of more efficient drug variants having lower side effects.

We have investigated the effect of some active principles (mainly Ibuprofen and Benzocaine) on bilayer membranes composed of L-α-phosphatidylcholine (SoyPC). Structure and evolution of SoyPC lipid bilayers in the presence of drugs have been characterized by means of reflectivity, grazing incidence and small angle scattering of neutrons. Dynamics of SoyPC membranes has been studied through neutron spin echo spectroscopy.

It has been observed that ibuprofen induces a two-step structuring behavior in the SoyPC films, where the structure evolves from the purely lamellar phase for pure SoyPC over a superposition of two hexagonal phases to a purely hexagonal phase at high concentrations. A stiffening of the membrane is observed upon addition of ibuprofen. This behavior may be instrumental in explaining the toxic behavior of ibuprofen in long-term application.

Addition of benzocaine to pure SoyPC bilayers promotes a destabilization of the membrane assembly by inducing a progressive thickening of the bilayer region, as well as the formation of ruptures in the membrane. It may be argued a correlation between the arrangement of the phospholipid membrane and the drug cytotoxicity, as any structural modification is a change of the unperturbed configuration of a cell membrane.

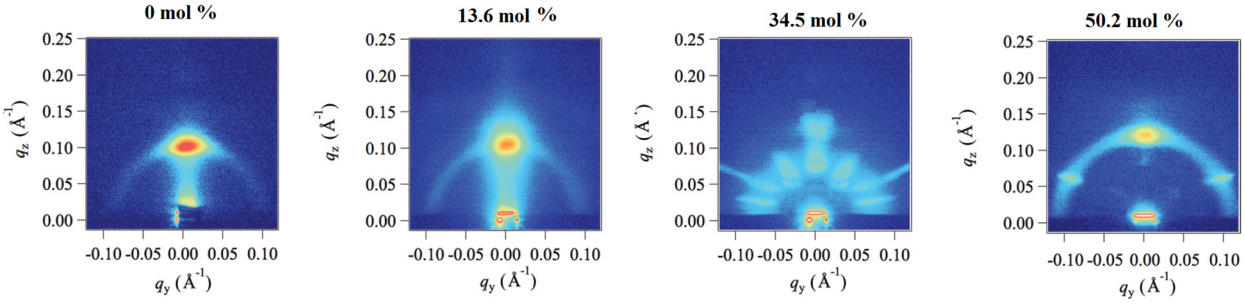

Figure 1 GISANS detector images at an incident angle of 0.2° (below the critical angle, at λ = 5Å) at various concentrations of ibuprofen reported above. Concentrations are expressed as mole percentage with respect to the total solute amount .Data simulation shows the presence of two different hexagonal lattices at 34.5 mol % amount of ibuprofen. These structures are stabilized against each other by a primitive tetragonal lattice. At very high concentrations (50.2 mol %) only a hexagonal structure with an axis parallel to the substrate is retained.