

**Phenothiazine derivative causes phase separation in phosphatidylethanolamine model membranes**

Olga Wesołowska, Andrzej B. Hendrich, Noboru Motohashi, Krystyna Michalak

Phenothiazine derivatives are known as popular antipsychotic drugs and effective multidrug resistance modulators. The interactions of newly synthesised phenothiazine derivative: 2-trifluoromethyl-10-(4-[methylsulfonylamid] buthyl)-phenothiazine with dimyristoylphosphatidylethanolamine (DMPE) was studied by means of microcalorimetry. The drug caused decrease of phospholipid main phase transition temperature. In the range of 0.04–0.1 drug/lipid mole ratio the phase separation was observed. The transition enthalpy change was diminished in the presence of drug, however it stayed fairly constant in the concentration range in which phase separation occurred. The most likely reasons of phase separation in DMPE–phenothiazine derivative system are different spatial orientations that drug molecules might adopt inside the model membrane. It is apparently connected with different kinds of drug's interaction with the hydrogen bonds network crosslinking polar region of DMPE bilayer.