

**A NEW PHENOTHIAZINE DERIVATIVE ALTERS THE FLUIDITY AND
THERMOTROPIC BEHAVIOUR OF PHOSPHATIDYLCHOLINE
MODEL MEMBRANES**

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Phenothiazine derivatives, widely used as effective tranquilizers, have lately attracted attention as effective multidrug resistance modulators. The interactions of a newly synthesised phenothiazine derivative, 2-trifluoromethyl-10-(4-[methylsulfonylamid]butyl)-phenothiazine (FPhMS), with phosphatidylcholine model membranes were studied by means of microcalorimetry and fluorescence spectroscopy. FPhMS showed a biphasic effect on the DPPC main phase transition parameters. The transition temperature and enthalpy change decreased up to a drug:lipid molar ratio of 0.06, and then increased above this concentration. FPhMS also caused a gradual broadening of transition peaks for all the concentrations studied. DPH (1,6-diphenyl-1,3,5-hexatriene) polarization measurements showed that the phenothiazine derivative caused a decrease in bilayer order in the liquid crystalline state and an increase in the gel state. Fluorescence spectroscopy also revealed that FPhMS at a concentration of 100 μ M influenced the DPPC main phase transition parameters: its melting temperature was decreased and the transition range was broadened. It was concluded that the phenothiazine derivative exerts a cholesterol-like effect on the model membrane and at higher concentrations induces a new mode of bilayer packing. Similarly to cholesterol, the FPhMS molecule also possesses a rigid aromatic ring system, and is probably located near the hydrophilic/hydrophobic interface of lipid leaflet. Like the liquid-ordered phase induced by cholesterol at high concentrations, FPhMS:DPPC mixtures are characterised by low cooperativity and reduced molecule mobility compared to pure lipid.

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