The Effect of Cholesterol and Etomidate Interactions on the Physical Behaviour of Phospholipid Dispersions Measured by Intramolecular Excimer Fluorescence

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Recently we have introduced the intramolecular excimer forming probe 1,3-bis(β-naphthyl)propane (ββDNP) to monitor changes in the pyhsical behaviour of phospholipid dispersions (Dangreau et al. 1979). The ratio of excimer to monomer intensities (I_E/I_M) is sensitive to changes in the "microfluidity" of lipid bilayers.

Using this intramolecular excimer forming system, at a ββDNP to lipid molar ratio of 0.01, we now describe the interaction at pH 7.4 (phosphate buffer 50 mM) of dimyristoylphosphatidylcholine (DMPC) dispersions with cholesterol and with the hypnotic agent etomidate hydrochloride, R-(+)ethyl 1-(1-phenylethyl)-1H-imidazole-5-carboxylate monohydrochloride, a product synthetised by Janssen Pharmaceutica Belgium. The effects of both components were studied as a function of temperature and concentration.
In the case of cholesterol large multilamellar liposomes were used. Over the entire temperature range studied, the ratio I_E/I_M decreases with increasing cholesterol content. Addition of cholesterol eliminates the pretransition while melting of the hydrocarbon layer seems to occur over a wider range.
With etomidate small unilamellar DMPC vesicles were used. Above the transition temperature the ratio I_E/I_M is diminished, indicating a reaction of the "microfluidity". However with increasing etomidate concentration, the transition moves to lower temperatures. These results suggest that etomidate not only changes the lipid chain packing by interdigitation but also interacts electrostatically with the polar headgroups of the lipids (Cater et al. 1974). These preliminary observations could lead to an understanding of the pharmacological properties of etomidate.
Our experiments demonstrate that intramolecular excimer forming probes are sensitive to interactions of cholesterol and etomidate with lipid dispersions.

1. Cater, B., Chapman, D., Hawes,S. and Saville, J. (1974) Biochim. Biophys. Acta 363, 54 - 69.
2. Dangreau, H., Joniau, M. and De Cuyper, M. (1979)Biochem. Biophys. Res. Commun. 87, 468 - 478.