Interaction of Enkephalins and Anti-Malarial Drugs with Lipid Model Membranes

Basso, L.G.M.[1], Naal, R.M.Z.[2], Costa-Filho, A.J.[1]

[1] Instituto de Física de São Carlos, Universidade de São Paulo
[2] Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo

Leu-Enkephalinamide (Leu-EN) and Met-Enkephalinamide (Met-EN) are peptides with morphine-like activity. Primaquine Diphosphate (PDP) and Chloroquine Diphosphate (CDP) are therapeutic agents used in the treatment of malaria. Interaction of these small molecules with phospholipid vesicles is pivotal for understanding their biological activity. We investigated the effects of drug binding on the lipid phase transition and acyl chain dynamics by Electron Spin Resonance. Labels located at different positions along the lipid acyl chain were used to monitor these regions of the membrane. Our results indicated that both peptides increase bilayer packing and headgroup mobility. The interaction of Leu-EN with DPPC vesicles causes greater alterations on membrane structure than Met-EN. The main phase transition temperature (Tm) of DPPC bilayers was lowered by 0.4ºC and 0.7ºC in the presence of Met-EN and Leu-EN, respectively. Interaction of PDP and CDP with DMPC dispersions showed a slight increase of the membrane packing in DMPC gel phase. Our data indicate that PDP is more effective in changing the membrane structure than CDP. Furthermore, the CDP effect on structure and dynamics of model membranes is more pronounced near the polar headgroup, while PDP effects are more pronounced close to the membrane center. The phase transition temperature for DMPC bilayers were lowered by 4^{o}C in the presence of PDP, whereas CDP did not alter Tm significantly. These results suggest that PDP and Leu-EN promote stronger changes in the hydrophobic region of the bilayer than CDP and Met-EN. The results were discussed in terms of the ligand chemical structures. Acknowledgments: FAPESP, CNPq. Keywords: ESR, model membrane, enkephalin, anti-malarial drugs.