Polymodal Dose- Effect of Synthetic Antioxidant (Phenozan K) on Lipid Oxidation and Microviscosity of Microsomal Membranes

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The synthetic phenolic antioxidant - β-(4-hydroxy-3,5-ditret-butylphenyl) propionic acid potassium salt (K) or phenozan K (PhK) possesses a wide biological activity. The microsomal membranes are classical model to study a spontaneous lipid peroxidation (LPO). In the present work we investigated the effect of PhK in a wide range of concentration (from high to ultra-low concentrations) on LPO and lipid microviscosity of microsomal membranes isolated from liver of mice. The aqueous solutions of PhK were prepared by successive dilutions in the range of concentration 10^{-2}-10^{-16} M. The lipid microviscosity was studied by EPR-technique on the computerized spectrometer Bruker-EMX using spin-probes16-doxyl-stearic acids (16-DSA). The microviscosity value of the hydrophobic lipid regions estimated by rotation correlation time (τ_c) of 16-DSA from EPR-spectra obtained. The extent of LPO determined by content of malonic dialdehyde (MDA). It was found the nonlinear dependences of value of τ_c of 16-DSA and MDA content on the concentration of PhK. It was observed three “waves” of increase of microviscosity: first 10^{-4} M explained by incorporation of PhK into the membrane lipids; second - 10^{-10} M can be related with formation of the micro-domains or changes of them, and third at ultra-low concentration (ULC) - 10^{-14} M can be related with formation of nanoassociates. It was found a correlation between changes of lipid microviscosity of membranes and conductivity of solutions in the range of ULC of PhK – 10^{-13} -10^{-17} M. PhK inhibited LPO in membranes in the range of concentration 10^{-6}-10^{-18} M, maximum (100-80%) at 10^{-11}M and 10^{-15} M. It was shown the correlation between changes of LPO inhibition and microviscosity value under the effect of PhK at the concentration 10^{-4} -10^{-18} M. It was concluded that polymodal effect of PhK in a wide range of concentration on microsomal membranes is typical to “dose-effect “ dependences of drugs affecting at ULC. The results obtained can be important to understand the mechanism of action of this antioxidant in membranes.