Ostroumova O.S., Efimova S.S., Schagina L.V. 2011. 5- and 4'-hydroxylated flavonoids affect voltage gating of single alpha-hemolysin pore. Biochim. Biophys. Acta. V. 1808. P. 2051.

Ostroumova O.S., Efimova S.S., Schagina L.V. 2012b. Probing amphotericin B single channel activity by membrane dipole modifiers. PLoS One. V. 7. P. 30261. https://doi.org/10.1371/journal.pone.0030261

Ostroumova O.S., Gurnev P.A., Schagina L.V., Bezrukov S.M. 2007a. Asymmetry of syringomycin E channel studied by polymer partitioning. FEBS Letters. V. 581. P. 804.

Ostroumova O.S., Kaulin Y.A., Gurnev A.P., Schagina L.V. 2007б. Effect of agents modifying the membrane dipole potential on properties of syringomycin E channels. Langmuir. V. 23. P. 6889.

Ostroumova O.S., Malev V.V., Ilin M.G., Schagina L.V. 2010. Surfactin activity depends on the membrane dipole potential. Langmuir. V. 26. P. 15092.

Rokitskaya T.I., Kotova E.A., Antonenko Y.N. 2002. Membrane dipole potential modulates proton conductance through gramicidin channel: movement of negative ionic defects inside the channel. Biophys. J. V. 82. P. 865.

Sultana S., Asif H.M. 2017. Review: medicinal plants combating against hypertension: a green antihypertensive approach. Pak. J. Pharm. Sci. V. 30. P. 2311.

Svetina S., Kuzman D., Waugh R.E., Ziherl P., Zeks B. 2004. The cooperative role of membrane skeleton and bilayer in the mechanical behaviour of red blood cells. Bioelectrochem. V. 62. P. 107.

Swain J., Kumar Mishra A. 2015. Location, partitioning behavior, and interaction of capsaicin with lipid bilayer membrane: study using its intrinsic fluorescence. J. Phys. Chem. B. V. 119. P. 12086.

Torrecillas A., Schneider M., Fernández-Martínez A.M., Ausili A., de Godos A.M., Corbalán-García S., Gómez-Fernández J.C. 2015. Capsaicin fluidifies the membrane and localizes itself near the lipid-water interface. ACS Chem. Neurosci. V. 6. P. 1741.

Winski S.L., Carter D.E. 1998. Arsenate toxicity in human erythrocytes: characterization of morphologic changes and determination of the mechanism of damage. J. Toxicol. Environ. Health A. V. 53. P. 345.

Yamaguchi K., Kato M., Suzuki M., Asanuma K., Aso Y., Ikeda S., Ishigai M. 2011. Pharmacokinetic and pharmacodynamic modeling of the effect of an sodium-glucose cotransporter inhibitor, phlorizin, on renal glucose transport in rats. Drug. Metab. Dispos. V. 39. P. 1801.

Yan L.L., Zhang Y.J., Gao W.Y., Man S.L., Wang Y. 2009. *In vitro* and *in vivo* anticancer activity of steroid saponins of paris polyphylla var. Yunnanensis Exp. Oncol. V. 31. P. 27.

Yassin A.M., El-Deeb N.M., Metwaly A.M., Fawal G.F., Radwan M.M., Hafez E.E. 2013. Induction of apoptosis in human cancer cells through extrinsic and intrinsic pathways by balanites Aegyptiaca furostanol saponins and saponin-coated silvernanoparticles. Der. Pharm. Lett. V. 182. P. 1675.

THE DISORDERING EFFECT OF PLANT METABOLITES ON MODEL LIPID MEMBRANES OF VARIOUS THICKNESS

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The effects of different plant metabolites, phloretin, capsaicin, digitonin, diosgenin, and betulin, on the model lipid membranes was studied. The method of the measuring the leakage of the fluorescent marker calcein from the liposomes and the differential scanning microcalorimetry of the lipid vesicle suspension were performed. It was found that the calcein release from palmitoyloleoylphosphocholine (POPC) liposomes at the addition of the tested metabolites in a ratio of 1 to 50 to lipid decreased in the order of capsaicin > phloretin ⩾ betulin ≈ diosgenin ≈ digitonin. Moreover, in the cholesterol and ergosterol-containing POPC liposomes the activity decreased in the order of diosgenin ≈ digitonin > betulin > capsaicin > phloretin. The ability of phloretin and capsaicin to significantly reduce the melting temperature (T_m) and to increase the half-width of the main peak on the endotherm ($T_{1/2}$) of dipalmitoylphosphocholine (DPPC), distearoylphosphocholine (DSPC) and diarachidoylphosphocholine (DAPC) was shown. The results indicated that these molecules were able to incorporate between the polar lipid "head" groups and to increase the mobility of the hydrocarbon chains. It was found that the increase in the length of the saturated chains of the membrane-forming lipids (from 16 to 20 hydrocarbon units) caused the decrease and increase in the absolute values of ΔT_m and $\Delta T_{1/2}$ in the cases of phloretin and capsaicin respectively. This fact indicated the difference in the localization of phloretin and capsaicin in the membrane. Steroid saponins weakly affected the thermotropic behavior of phosphocholines: the absolute values of ΔT_m and $\Delta T_{1/2}$ decreased in the order of DPPC, DSPC and DAPC and increased in the order of betulin, diosgenin, digitonin. Steroid saponins were characterized by the more pronounced effects on the thermotropic behavior of the sterol-phospholipid mixture. The results obtained were consistent with the assumption of the higher affinity of the tested saponins to sterol-containing membranes than to bilayers made from pure phospholipids.

Keywords: plant metabolites, small molecules, polyphenols, saponins, alkaloids, lipid membranes, liposomes