J Membrane Biol (2014) 247:739–745
DOI 10.1007/s00232-014-9703-7

The Influence of Halogen Derivatives of Thyronine and Fluorescein on the Dipole Potential of Phospholipid Membranes

Svetlana S. Efimova · Ludmila V. Schagina · Olga S. Ostroumova

Received: 29 April 2014 / Accepted: 27 June 2014 / Published online: 15 July 2014

Abstract The effects of halogen derivatives of thyronine (tetraiodotironine and triiodothyronine) and fluorescein (Rose Bengal, phloxine B, erythrosin, eosin Y, and fluorescein) on the dipole potential of membranes composed of diphytanoylphosphocholine, diphytanoylphosphoserine, and diphytanoylphosphoethanolamine were investigated. A quantitative description of the modifying action of the agents was presented as characteristic parameters of the Langmuir adsorption isotherm: the maximum changes in the dipole potential of the membrane at an infinitely high concentration of modifiers and the desorption constant, characterizing their inverse affinities to the lipid phase. It was shown that the iodine-containing hormones led to a less significant reduction in the dipole potential of phospholipid membranes compared to the xanthene dyes, Rose Bengal, phloxine B, and erythrosin. The latter were characterized by the highest affinity for the lipid membranes compared to tetraiodotironine and triiodothyronine. It was found that the effect of iodine-containing hormones and xanthene dyes on the membrane dipole potential was caused by their uncharged and charged forms, respectively.

Keywords Iodine-containing hormones · Xanthene dyes · Phospholipids · Membrane dipole potential · Planar lipid bilayers

S. S. Efimova (✉) · L. V. Schagina · O. S. Ostroumova
Institute of Cytology of the Russian Academy of Sciences, Tikhoretsky Ave. 4, St. Petersburg 194064, Russia
e-mail: ssefimova@mail.ru

Introduction

The dipole potential of model and cell membranes (φ_d) is the difference in electric potential between the polar exterior of the lipid bilayer and its hydrocarbon interior. This potential drop originates from the specific orientation of polar lipid residues and water dipoles at the membrane-solution interface (Liberman and Topaly 1969; Hladky and Haydon 1973; Brockmann 1994). The hydrocarbon core is more positive relative to the water phase bathing the membrane. The membrane dipole potential depends on the lipid composition of the membrane. It is known that φ_d influences membrane transport (Malkov and Sokolov 1996; Busath et al. 1998; Hwang et al. 2003; Duffin et al. 2003; Karlovska et al. 2006; Luchian and Mereuta 2006; Ostroumova et al. 2007, 2008, 2010, 2012a, b, 2014; Mereuta et al. 2008; Ostroumova and Schagina 2009).

The adsorption of amphiphilic molecules called dipole modifiers, which have a significant dipole moment and a preferred orientation at the boundary of the membrane, leads to changes in the magnitude of the membrane dipole potential (Brockmann 1994; Lairion and Disalvo 2004). Some plant polyphenols (Andersen et al. 1976; Cseh and Benz 1998; Sokolov and Mirsky 2004; Efimova and Ostroumova 2012; Ostroumova et al. 2013a, b) and styryl dyes (Malkov and Sokolov 1996; Efimova and Ostroumova 2012) can cause significant changes in the membrane dipole potential. The structural features of these dipole modifiers, which are responsible for the changes in the membrane dipole potential, have been identified. In particular, it has been shown that the iodine-containing hormones, thyroxine and triiodothyronine, (Tsybulskaya et al. 1984; Issé et al. 2013) and the xanthene dye Rose Bengal (Kotova et al. 2000; Efimova and Ostroumova 2012) reduce the dipole potential of phospholipid bilayers, but the

relationship between the structural aspects of these dipole modifiers and the magnitude of the membrane dipole potential has not yet been established.

The iodine-containing hormones, thyroxine and triiodothyronine are the main thyroid hormones that play a key role in the regulation of metabolism. The chemical structures of these hormones represent interconnected benzene hydrophobic rings. The thyroxine molecule contains 4 atoms of iodine whereas triiodothyronine contains 3 iodine atoms per molecule. There is evidence to show that the thyroid hormones are normal constituents of biological membranes in vertebrates and that some of the physiological effects of these hormones actually occur in the membranes (Hulbert 2000). Thyroid hormones are able to interact with plasma membranes and modify membrane fluidity (Farias et al. 2006; Issé et al. 2013). Electronic spin resonance measurements using spin-labeled liposomes indicated that thyroxine can penetrate the lipid core region of liposomes (Issé et al. 2003), suggesting that both hydrophobic rings are close to the lipid core, whereas the more hydrophilic and ionizable region of the thyroxine formed by the amino and the carboxyl groups of the alanine residue is at the membrane-aqueous interface (Issé et al. 2003). Tsybulskaya et al. (1984) have shown that the iodine-containing hormones reduce the dipole potential of a cholesterol-containing lecithin bilayer. Using nonactin and hydrophobic anions, the authors demonstrated that the influence of thyroxine and triiodothyronine on the φ_d is practically the same and is not caused by the sorption of the negatively charged form of the hormones. Rather, the observed effects resulted from the adsorption of the uncharged form of triiodothyronine. Using differential scanning calorimetry, (Issé et al. 2013) demonstrated that thyroxine, triiodothyronine, and diiodotironin reduce the dipole potential of dipalmitoyloleoylphosphocholine and palmitoyloleoylphosphocholine bilayers. (Issé et al. 2003) showed that the effectiveness of the reduction in the diphytanoylphosphocholine bilayer dipole potential progressively decreases for tetraiodtironin, triiodothyronine, and diiodotironin in order. (Issé et al. 2013) associated the effectiveness of the reduction in the membrane dipole potential with the immersion depth of the hormone molecules in the hydrocarbon region of the bilayer and the ability to affect the ordering of lipid molecules in the membrane.

Fluorescein is the basic representative of the class of xanthene dyes. Other xanthene dyes are the halogen derivatives of fluorescein. Erythrosin is the 4-iodine-derivative of fluorescein, eosin Y is the 4-bromo-derivative of fluorescein, Rose Bengal is the 4-chloro-4-iodo-derivative of fluorescein, and phloxine B is the 4-chloro-4-bromo-derivative of fluorescein. The xanthene dyes are often used as fluorescent nanomarkers to study the binding of biological objects with various ligands. Decraene et al. (2006) demonstrated the ability of a cellulose acetate coating containing Rose Bengal to kill microbes (*Staphylococcus aureus*, *Escherichia coli*, *Clostridium difficile*, and *Candida albicans*). The influence of xanthene dyes on the physicochemical properties of the lipid bilayer, in particular, on the membrane dipole potential and the packing density of the lipid molecules in the bilayer, should be considered in assessing their biological action.

Kotova et al. (2000) assumed that the adsorption of Rose Bengal on the bilayer-solution interface leads to a reduction of the dipole potential drop at the membrane-solution boundary. Efimova and Ostroumova (2012) showed that the maximum change in the dipole potential of the diphytanoylphosphocholine-membrane at an infinitely high concentration of Rose Bengal is equal to 121 ± 9 mV. At the same time, the influence of other xanthene dyes (phloxine B, erythrosine, eosin Y, and fluorescein) on the magnitude of the dipole potential of phospholipid membranes has not yet been investigated.

The aim of the study was to identify structural features of iodine-containing hormones and xanthene dyes responsible for the reduction in the magnitude of the membrane dipole potential. We have identified new dipole modifiers, phloxine B, and erythrosin, and determined quantitative characteristics of their influence on the magnitude of the dipole potential of phospholipid bilayers. The molecular mechanisms of the observed effects have been proposed.

Materials and Methods

All chemicals were of reagent grade. Synthetic 1,2-diphytanoyl-*sn*-glycero-3-phosphocholine (DPhPC), 1,2-diphytanoyl-*sn*-glycero-3-phosphoserine (DPhPS), and 1,2-diphytanoyl-*sn*-glycero-3-phosphoetanolamine (DPhPE) were obtained from Avanti Polar Lipids, Inc. (Pelham, AL). L-thyroxine (3,3′,5,5″-tetraiodo-L-thyronine), 3,3′,5′-triiodo-L-thyronine, Rose Bengal (4,5,6,7-tetrachloro-2′,4′,5′,7′-tetraiodofluorescein disodium salt), phloxine B (4,5,6,7-tetrabromo-2′,4′,5′,7′-tetrachlorofluorescein disodium salt), erythrosine (2′,4′,5′,7′-tetraiodofluorescein disodium salt), eosin Y (2′,4′,5′,7′-tetrabromofluorescein), fluorescein, DMSO, KCl, HEPES, and MES were purchased from Sigma Chemical (St. Louis, MO, USA). Water was distilled twice and deionized. Solutions of 0.1 M KCl were buffered using 5 mM HEPES at pH 7.4 and 5 mM MES at pH 2.5. The ionophore, nonactin (NonA), was purchased from Sigma Chemical (St. Louis, MO, USA). The chemical structures of phospholipid molecules are shown in Fig. 1. The chemical structures of iodine-containing hormones and xanthene dyes are shown in Table 1.

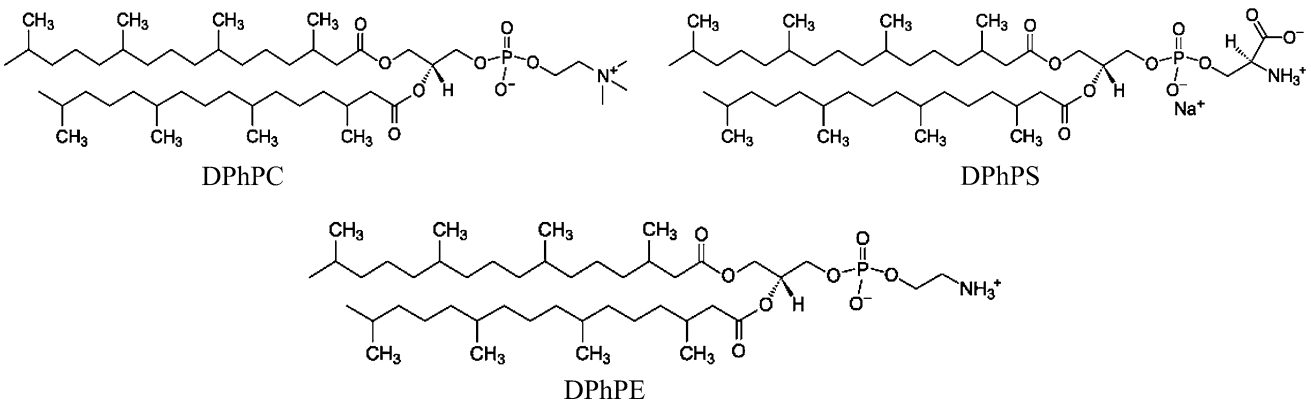
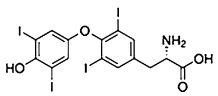
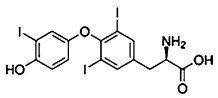
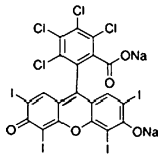
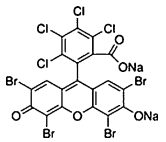
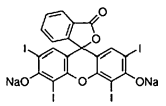
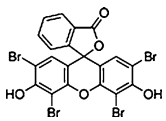
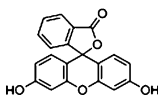


Fig. 1 Chemical structures of the membrane lipids DPhPC, DPhPS, and DPhPE

Table 1 Characteristic parameters of the Langmuir isotherm for the adsorption of halogen derivatives of thyronine and fluorescein on the phospholipid bilayers

Halogen derivatives		Chemical structure	Parameter	Membrane composition		
				DPhPC	DPhPS	DPhPE
Iodine-containing hormones	Thyroxine		$-\Delta\varphi_d(\infty)$, mV	61 ± 7	55 ± 7	58 ± 5
			K, μM	3.5 ± 0.1	2.1 ± 0.1	4.9 ± 0.3
	Triiodothyronine		$-\Delta\varphi_d(\infty)$, mV	58 ± 9	57 ± 5	54 ± 5
			K, μM	5.3 ± 0.2	2.0 ± 0.1	5.3 ± 0.5
Xanthene dyes	Rose Bengal		$-\Delta\varphi_d(\infty)$, mV	121 ± 9[a]	12 ± 3	35 ± 4
			K, μM	0.2 ± 0.1[a]	0.5 ± 0.1	1.3 ± 0.1
	Phloxine B		$-\Delta\varphi_d(\infty)$, mV	83 ± 4	17 ± 7	70 ± 7
			K, μM	0.2 ± 0.1	1.0 ± 0.1	1.2 ± 0.1
	Erythrosin		$-\Delta\varphi_d(\infty)$, mV	65 ± 6	3 ± 2	51 ± 7
			K, μM	0.8 ± 0.1	2.3 ± 0.1	0.5 ± 0.1
	Eosin Y		$-\Delta\varphi_d(\infty)$, mV	5 ± 2	6 ± 2	15 ± 3
			K, μM	0.4 ± 0.1	0.2 ± 0.1	0.6 ± 0.1
	Fluorescein		$-\Delta\varphi_d(\infty)$, mV	6 ± 2	12 ± 5	10 ± 3
			K, μM	0.4 ± 0.1	0.7 ± 0.1	0.3 ± 0.1

The membranes were constructed using DPhPC, DPhPS, and DPhPE and bathed in 0.1 M KCl at pH 7.4. $V = 50$ mV

[a] The results are from (Efimova and Ostroumova 2012)

Lipid membranes were made from phospholipids containing saturated hydrocarbon chains (DPhPC, DPhPS, and DPhPE) to exclude the possibility of lipid oxidation under the influence of photosensitizers (Kotova et al. 2000). Such lipid compositions are more appropriate for modeling of the cell phospholipid membranes due to the similar density of lipid packing in the membrane (Hsieh et al. 1997).

Virtually solvent-free planar lipid bilayers were prepared using a monolayer-opposition technique (Montal and Muller 1972) on a 50-μm-diameter aperture in a 10-μm-thick Teflon film separating two (*cis* and *trans*) compartments of a Teflon chamber. The aperture was pretreated with hexadecane. Lipid bilayers were made from DPhPC, DPhPS, and DPhPE from stock solutions in pentane (1, 2, and 5 mg/ml, respectively). After the membrane was completely formed and stabilized, NonA from a stock solution (7 μg/ml in ethanol) was added to both compartments to obtain a final concentration ranging from 0.1 to 10.0 μM. Ag/AgCl electrodes with agarose/2 M KCl bridges were used to apply the transmembrane voltage (V) and measure the transmembrane current (I).

Ion currents were measured using an Axopatch 200B amplifier (''Axon Instruments'') in the voltage-clamp mode. Data were digitized using a Digidata 1440A and analyzed using pCLAMP 10.0 (''Axon Instruments'') and Origin 8.0 (''Origin Lab''). The conductance of the lipid bilayer (G) was determined at a constant transmembrane voltage ($V = 50$ mV).

The steady-state conductance of K^+-NonA was modulated via the two-sided addition of iodine-containing hormones (thyroxine and triiodothyronine) or xanthene dyes (Rose Bengal, phloxine B, erythrosine, eosin Y and fluorescein) from mM stock solutions in ethanol or DMSO to the membrane-bathing solution at final concentrations ranging from 2 to 50 μM or 0.25 to 10.00 μM, respectively. The final concentration of ethanol or DMSO in the chamber did not exceed 0.2 %. At this concentration, the solvents do not disturb the integrity and stability of the membrane and do not influence the conductance of the lipid bilayer.

The changes in the φ_d ($\Delta\varphi_d$) were calculated by assuming that the membrane conductance is related to φ_d by the Boltzmann distribution as follows (Andersen et al. 1976):

$$\frac{G_m}{G_m^0} = \exp\left(-\frac{q_e \Delta\varphi_d}{kT}\right) \quad (1)$$

where G_m and G_m^0 are the steady-state membrane conductances induced by NonA in the presence and absence of dipole modifiers, respectively; q_e is the electronic charge; k is the Boltzmann constant, and T is the temperature in degrees Kelvin. It is assumed that the ion's concentration in the aqueous phase and ion mobility within the hydrocarbon region of the bilayer stay the same.

The changes in the φ_d for defined experimental conditions were averaged from 3 to 5 bilayers (mean ± SD).

A Langmuir adsorption isotherm was used to describe the adsorption of iodine-containing hormones and xanthene dyes to lipid bilayers as a first-order approximation (Efimova and Ostroumova 2012):

$$\Delta\phi_d(C) = \frac{\Delta\varphi_d(\infty)}{C + K}, \quad (2)$$

where $\Delta\varphi_d(C)$ is the dipole potential changes at concentration C of the dipole modifier, $\Delta\varphi_d(\infty)$ is the maximum potential change, and K is the desorption constant, which provides a meaningful measure of the inverse affinity between the modifier and the lipid. The dissociation constant was determined as the slope of a linear dependence of $[\Delta\varphi_d(\infty)]/[\Delta\varphi_d(C)]$ on 1/C. The linear fitting of the indicated dependences was performed using Origin 8.0 (''Origin Lab''). The errors of $\Delta\varphi_d(\infty)$ and K were determined as the maximum measurement error of $\Delta\varphi_d$ (C) and the error of $[\Delta\varphi_d(\infty)]/[\Delta\varphi_d(C)]$, respectively.

Results and Discussion

Figure 2 illustrates the dependences of the $|\Delta\varphi_d|$ of phospholipid bilayers on the concentration of iodine-containing hormones and xanthene dyes. The presented curves are tend to saturation at large concentrations of the agents. Figure 2a–c shows that iodine-containing hormones, thyroxine, and triiodothyronine reduce the dipole potential of various phospholipid membranes in a similar manner. Figure 2d–f demonstrates that the effect of xanthene dyes on the dipole potential of phospholipid membranes depends on the head group of lipid molecules of the membrane. Rose Bengal decreases the dipole potential of DPhPC membranes (Fig. 2d) while it does not practically change the φ_d of negatively charged DPhPS bilayers (Fig. 2e). One can see that the effect of Rose Bengal on the dipole potential of DPhPE bilayers (Fig. 2f) is smaller than its effect on DPhPC membranes. Phloxine B is equally effective in the reduction of the dipole potential of DPhPC and DPhPE bilayers (Fig. 2d, f), and it does not change the φ_d of DPhPS bilayers (Fig. 2e). Erythrosin reduces the φ_d of DPhPC and DPhPE membranes and does not change the φ_d of DPhPS bilayers (Fig. 2d–f respectively). The effects of eosin Y and fluorescein on the dipole potential of DPhPC, DPhPS, and DPhPE bilayers are negligible (Fig. 2d–f respectively).

Earlier, we showed that the adsorption of Rose Bengal on the DPhPC bilayers is satisfactorily described by a Langmuir adsorption isotherm with characteristic parameters: the maximum changes in the dipole potential of the membrane at an infinitely high concentration of modifier ($-\Delta\varphi_d(\infty)$) and the desorption constant, characterizing its inverse affinity to the lipid phase (K) (Efimova and Ostroumova 2012). Figure 3 presents the dependences of $\Delta\varphi_d(\infty)/\Delta\varphi_d(C)$ on $1/C$ of thyroxine, triiodothyronine, Rose Bengal, phloxine B, erythrosine, eosin Y, and fluorescein in the DPhPC, DPhPS, and DPhPE bilayers. The

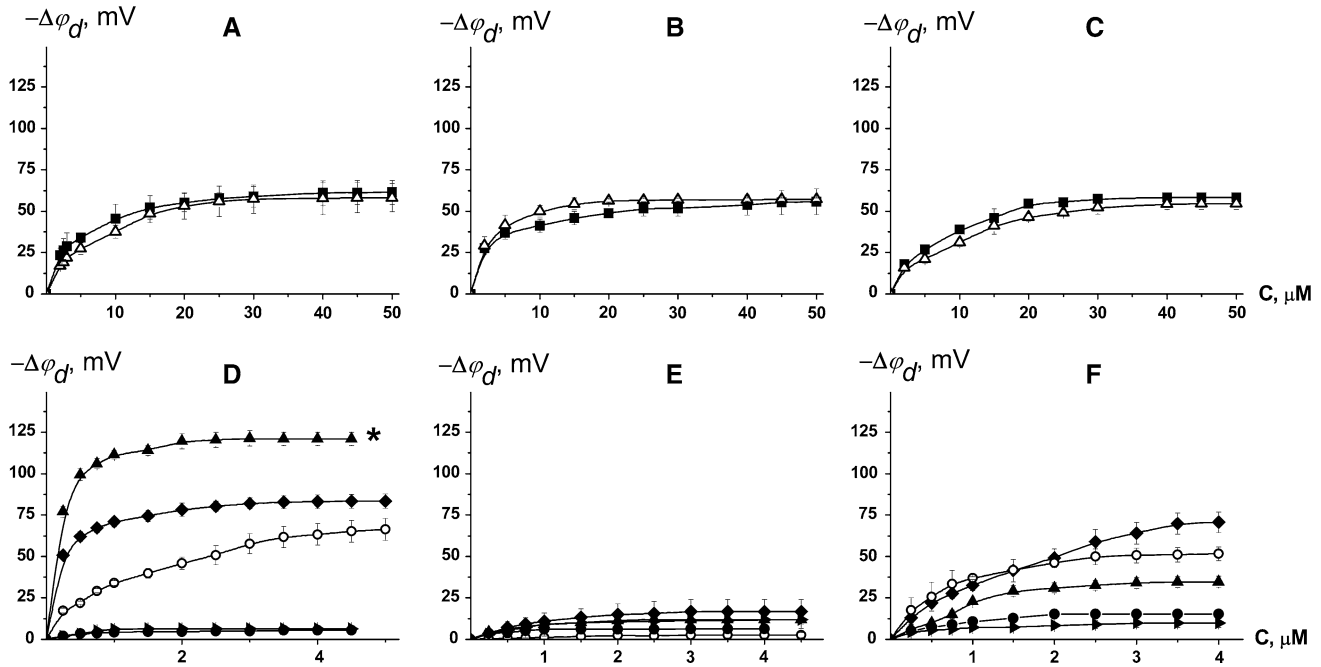


Fig. 2 The dependence of changes in the dipole potential of phospholipid membranes ($\Delta\varphi_d$) on various concentrations of thyroxine (*filled square*), triiodothyronine (*open triangle*), Rose Bengal (*up pointing closed triangle*), phloxine B (*diamond*), erythrosine (*open circle*), eosin Y (*closed circle*), and fluorescein (*right pointing closed triangle*). The membranes were constructed using DPhPC (**a**, **d**), DPhPS (**b**, **e**), and DPhPE (**c**, **f**) and bathed in 0.1 M KCl at pH 7.4. $V = 50$ mV. The results for the DPhPC bilayers for Rose Bengal are from (Efimova and Ostroumova 2012)

linearity of these dependences and the equality of the Y-intercepts to 1 clearly indicate the applicability of the Langmuir adsorption isotherm (2) for the approximation of the experimental data for other tested modifiers. The desorption constant can be determined as the slope of the indicated linear dependence of $\Delta\varphi_d(\infty)/\Delta\varphi_d(C)$ on $1/C$. Table 1 shows the characteristic parameters of the Langmuir adsorption isotherm, $-\Delta\varphi_d(\infty)$ and K, for different modifiers in the DPhPC, DPhPS, and DPhPE membranes. From Table 1, one can see that the maximum reduction in the φ_d of the phospholipid membrane due to the adsorption of thyroxine or triiodothyronine is equal to 60 ± 10 mV independent of membrane lipid composition. At the same time, the influence of xanthene dyes on the phospholipid membrane dipole potential is strongly affected by composition of lipid bilayers. The maximum decrease in the φ_d of DPhPC membranes due to addition of Rose Bengal in the membrane bathing solutions is equal to 121 ± 9 mV. The reduction in the dipole potential of the DPhPE bilayers is 3 times less than that of the DPhPC bilayers. The change in φ_d of the DPhPS bilayers due to Rose Bengal adsorption is equal to 12 ± 3 mV. Table 1 demonstrates that the maximum reduction in the dipole potential of the DPhPC, DPhPE, and DPhPS bilayers caused by phloxine B introduction in the membrane bathing solutions is equal to 83 ± 4, 70 ± 7, and 17 ± 7 mV, respectively. The approximation of the data presented in Fig. 2d–f gives $\Delta\varphi_d(\infty) = 65 \pm 6$ and 51 ± 7 mV for the erythrosin-modified DPhPC and DPhPE membranes, respectively. The data suggest that erythrosin does not significantly change the dipole potential of DPhPS bilayers. Eosin Y and fluorescein do not significantly affect the magnitude of the dipole potential of phospholipid bilayers (the maximum reduction in the φ_d is equal to 15 ± 3 mV).

The presented results demonstrate that the change in the magnitude of the membrane dipole potential due to the adsorption of iodine-containing hormones does not depend on the type and charge of the nitrogen base in the hydrophilic head of the phospholipid molecule. Therefore, the surface charge of the lipid bilayer does not influence the sorption of the hormones on the surface of the bilayer. These results are in agreement with the assumption of Tsybulskaya et al. (1984). According to Tsybulskaya et al. (1984), the effect of the iodine-containing hormones on the φ_d is due to the adsorption on the lipid bilayers of the uncharged form of the hormone molecules.

A comparison of the chemical structures of xanthene dyes and their effects on the dipole potential of phospholipid bilayers (see Table 1) allows one to conclude that the type of halogen substituent and its localization in the molecule are the main factors behind the observed effects. Comparison of erythrosin, eosin Y, and fluorescein indicates that halogen atoms of only iodine and not bromine impact the dipole modifier effect. The same conclusion

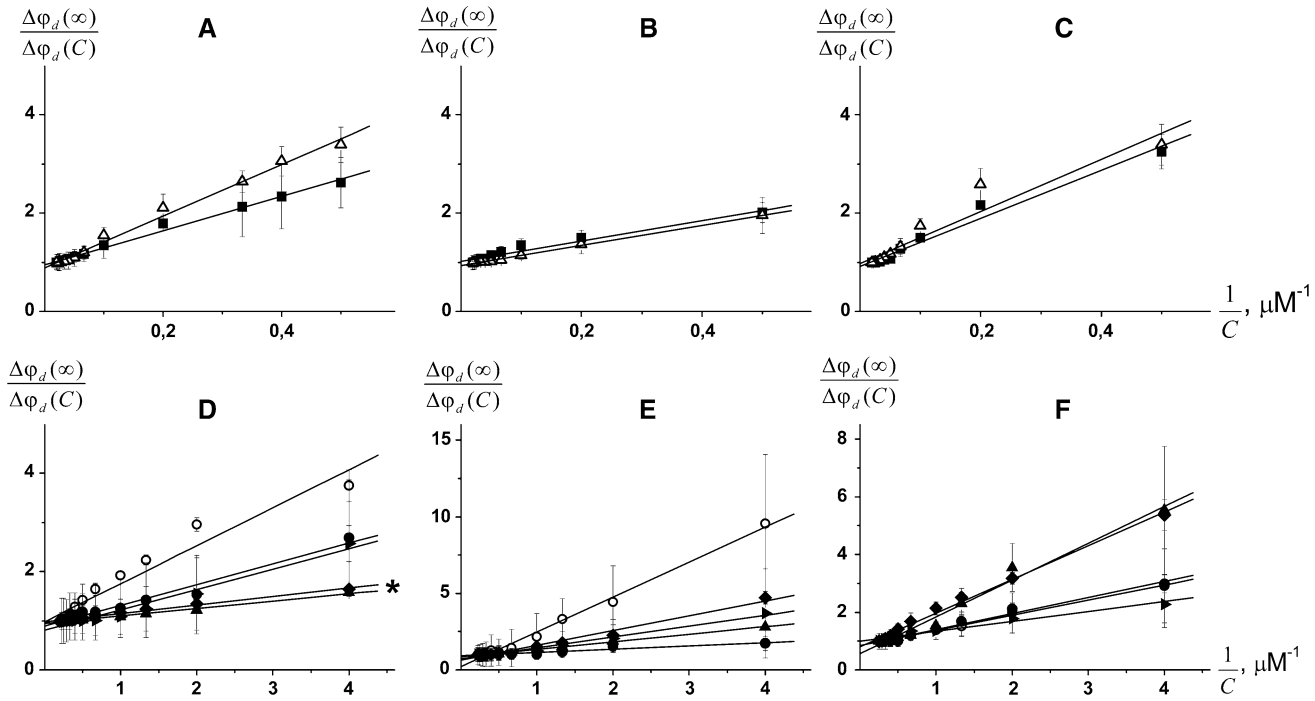


Fig. 3 The dependence of $[\Delta\varphi_d(\infty)]/[\Delta\varphi_d(C)]$ on $1/C$ for the conditions given in Fig. 2

may be drawn when Rose Bengal and phloxine B are compared. Comparison of Rose Bengal with erythrosin or phloxine B with eosin Y indicates that the presence of several chlorine atoms located near the carbonyl group significantly impacts the effect of xanthene dyes on the bilayer dipole potential.

From Table 1, one can see that Rose Bengal, phloxin B, and erythrosin are less effective in negatively charged DPhPS membranes compared with uncharged DPhPC and DPhPE bilayers. At physiological conditions (at pH 7.4), fluorescein and its derivatives have a negative charge (Batistela et al. 2011; Vlasova et al. 2011). It can be proposed that electrostatic repulsion between the negatively charged phospholipid molecules and the anionic form of the modifier, which is able to reduce the membrane dipole potential, may contribute to the observed effect.

To support this idea that anionic form of the xanthene dyes is able to decrease the magnitude of the membrane dipole potential while the neutral one does not change the φ_d we have employed the additional experiments at pH 2.5. It is known that xanthene dyes are not charged at pH 2.5 (Batistela et al. 2011; Vlasova et al. 2011). That is why xanthene dyes are expected to have no effect on the φ_d at pH 2.5. The results demonstrate that xanthene dyes, Rose Bengal, phloxin B, and erythrosin do not practically change the φ_d of DPhPC bilayers at pH 2.5 (the maximum reduction in the φ_d is equal to 1 ± 1 mV). Taking into account that the surface charge of DPhPC membranes is positive below pH 4 (Zhou and Raphael 2007; Chiriac and Luchian 2007; Mereuta et al. 2011), we also performed the experiments with DPhPS bilayers that are still negatively charged at defined conditions (Ivkov and Berestovski 1981). Rose Bengal does not affect the magnitude of the dipole potential of DPhPS-bilayers at pH 2.5 (the maximum reduction in the φ_d is equal to 0 ± 1 mV). Thus, data obtained supported the general scenario described before. One can think that the adsorption of the negatively charged form of these modifiers leads to a reduction in the membrane dipole potential.

The desorption constants, K, of the xanthene dyes are significantly less than that of iodine-containing hormones (Table 1). By consideration that K characterizes the inverse affinity of the modifier for the lipid, this means that xanthene dyes are characterized by an order of magnitude greater affinity to the lipid membranes compared with iodine-containing hormones.

The presented results clearly demonstrate that xanthene dyes, phloxine B, and erythrosin can significantly alter φ_d. The effect of xanthene dyes and iodine-containing hormones on the dipole potential of phospholipids bilayers is due to the adsorption of charged and uncharged forms of the modifier molecules, respectively.

Acknowledgments The work of Svetlana S. Efimova and Olga S. Ostroumova was partly supported by the Russian Foundation of Science (# 14-14-00565). The work of Ludmila V. Schagina was supported by the Program "Molecular and Cell Biology" of the Russian Academy of Sciences and SS-1721.2014.4.

References

Andersen OS, Finkelstein A, Katz I, Cass A (1976) Effect of phloretin on the permeability of thin lipid membranes. J Gen Physiol 67:749–771

Batistela VR, Pellosi DS, Souza FD, Costa WF, Santin SMO, Souza VR, Caetano W, Oliveira HPM, Scarminio IS, Hioka N (2011) pKa determinations of xanthene derivates in aqueous solutions by multivariate analysis applied to UV–Vis spectrophotometric data. Spectrochim Acta A 79:889–897

Brockmann H (1994) Dipole potential of lipid membranes. Chem Phys Lipids 73:57–79

Busath DD, Thulin CD, Hendershot RW, Phillips LR, Maughan P, Cole CD, Bingham NC, Morrison S, Baird LC, Hendershot RJ, Cotton M, Cross TA (1998) Noncontact dipole effects on channel permeation. I. Experiments with (5F-indole)Trp13 gramicidin A channels. Biophys J 75:2830–2844

Chiriac R, Luchian T (2007) pH modulation of transport properties of alamethicin oligomers inserted in zwitterionic-based artificial lipid membranes. Biophys Chem 130:139–147

Cseh R, Benz R (1998) The adsorption of phloretin to lipid monolayers and bilayers cannot be explained by Langmuir adsorption isotherms alone. Biophys J 74:1399–1408

Duffin RL, Garrett MP, Flake KB, Durrant JD, Busath DD (2003) Modulation of lipid bilayer interfacial dipole potential by phloretin, RH 421, and 6-ketocholestanol as probed by gramicidin channel conductance. Langmuir 19:1439–1442

Efimova SS, Ostroumova OS (2012) Effect of dipole modifiers on the magnitude of the dipole potential of sterol-containing bilayers. Langmuir 28:9908–9914

Farias RN, Fiore AM, Pedersen JZ, Incerpi S (2006) Nongenomic actions of thyroid hormones: focus on membrane transport systems. Immunol Endocr Metab Agents Med Chem 6:497–504

Hladky SB, Haydon DA (1973) Membrane conductance and surface potential. Biochim Biophys Acta 318:464–468

Hsieh CH, Sue SC, Lyu PC, Wu WG (1997) Membrane packing geometry of diphytanoylphosphatidylcholine is highly sensitive to hydration: phospholipid polymorphism induced by molecular rearrangement in the headgroup region. Biophys J 73(2):870–877

Hulbert AJ (2000) Thyroid hormones and their effects: a new perspective. Biol Rev Camb Philos Soc 75:519–631

Hwang TC, Koeppe RE, Andersen OS (2003) Genistein can modulate channel function by a phosphorylation-independent mechanism: importance of hydrophobic mismatch and bilayer mechanics. Biochemistry 42:13646–13658

Issé B, Fidelio G, Farías RN (2003) Thyroid hormones affect the membrane dipolar organization. Is it a general event in their non-genomic action? J Membr Biol 191(3):209–213

Issé BA, Yunes Quartino P, Fidelio GD, Farías RN (2013) Thyroid hormones-membrane interaction: reversible association of hormones with organized phospholipids with changes in fluidity and dipole potential. Chem Phys Lipids 175–176:131–137

Ivkov VG, Berestovski GN (1981) The dynamic structure of the lipid bilayer. Nauka, St. Petersburg, p 296

Karlovska J, Uhrikova D, Kucerka N, Teixeira J, Devinsky F, Lacko I, Balgavy P (2006) Influence of *N*-dodecyl-*N*, *N*-dimethylamine *N*-oxide on the activity of sarcoplasmic reticulum Ca(2+)-transporting ATPase reconstituted into diacylphosphatidylcholine vesicles: efects of bilayer physical parameters. Biophys Chem 119:69–77

Kotova EA, Rokitskaya TI, Antonenko YuN (2000) Two phases of gramicidin photoinactivation in bilayer lipid membranes in the presence of a photosensitizer. Membr Cell Biol 13:411–420

Lairion F, Disalvo EA (2004) Effect of phloretin on the dipole potential of phosphatidylcholine, phosphatidylethanolamine, and phosphatidylglycerol monolayers. Langmuir 20:9151–9155

Liberman EA, Topaly VP (1969) Permeability of bimolecular phospholipid membranes for fat-soluble ions. Biofizika (Russian) 14:452–461

Luchian T, Mereuta L (2006) Phlorizin- and 6-ketocholestanol-mediated antagonistic modulation of alamethicin activity in phospholipid planar membranes. Langmuir 22:8452–8457

Malkov DY, Sokolov VS (1996) Fluorescent styryl dyes of the RH series affect a potential drop on the membrane/solution boundary. Biochim Biophys Acta 1278:197–204

Mereuta L, Luchian T, Park Y, Hahm KS (2008) Single-molecule investigation of the interactions between reconstituted planar lipid membranes and an analogue of the HP(2-20) antimicrobial peptide. Biochem Biophys Res Commun 373:467–472

Mereuta L, Asandei A, Luchian T (2011) Meet me on the other side: trans-bilayer modulation of a model voltage-gated ion channel activity by membrane electrostatics asymmetry. PLoS ONE 6(9):e25276

Montal M, Muller P (1972) Formation of bimolecular membranes from lipid monolayers and study of their electrical properties. Proc Nat Acad Sci USA 65:3561–3566

Ostroumova OS, Schagina LV (2009) Effect of phloretin on sphingolipid-containing membranes modified by syringomycin E. Membr Cell Biol (Moscow) 3:281–285

Ostroumova OS, Kaulin YA, Gurnev AP, Schagina LV (2007) Effect of agents modifying the membrane dipole potential on properties of syringomycin E channels. Langmuir 23:6889–6892

Ostroumova OS, Schagina LV, Malev VV (2008) Effect of dipole potential of lipid bilayers on properties of ion channels formed by cyclic lipodepsipeptide syringomycin E. Membr Cell Biol (Moscow) 2:259–270

Ostroumova OS, Malev VV, Ilin MG, Schagina LV (2010) Surfactin activity depends on the membrane dipole potential. Langmuir 26:15092–15097

Ostroumova OS, Efimova SS, Chulkov EG, Schagina LV (2012a) The interaction of dipole modifiers with polyene-sterol complexes. PLoS ONE 7(9):e45135

Ostroumova OS, Efimova SS, Schagina LV (2012b) Probing amphotericin B single channel activity by membrane dipole modifiers. PLoS ONE 7(1):e30261

Ostroumova OS, Efimova SS, Schagina LV (2013a) Changes in the dipole potential of phospholipid membranes induced by the adsorption of flavonoids. Biophysics (In Russian) 58:474–480

Ostroumova OS, Efimova SS, Schagina LV (2013b) Phloretin induced reduction in dipole potential of sterol containing bilayers. J Membr Biol 246:985–991

Ostroumova OS, Efimova SS, Mikhailova EV, Schagina LV (2014) The interaction of dipole modifiers with amphotericin-ergosterol complexes. Effects of phospholipid and sphingolipid membrane composition. Eur Biophys J 43(4–5):207–215

Sokolov VS, Mirsky VM (2004) Electrostatic potentials of bilayer lipid membranes: basic research and analytical applications. In: Mirsky VM (ed) Ultrathin electrochemical chemo- and biosensors: technology and performance. Springer-Verlag, Heidelberg, pp 255–291

Tsybulskaya MV, Antonenko YuN, Tropsha AE, Yaguzhinsky LS (1984) Iodine-containing hormones dipole modifiers of phospholipid membranes. Biofizika 29:801–805 (in Russian)

Vlasova IM, Bukharova EM, Kuleshova AA, Saletsky AM (2011) Spectroscopic investigations of interaction of fluorescent nanomarkers of fluorescein family with human serum albumin at different values of pH. Curr Appl Phys 11:1126–1132

Zhou Y, Raphael RM (2007) Solution pH alters mechanical and electrical properties of phosphatidylcholine membranes: relation between interfacial electrostatics, intramembrane potential, and bending elasticity. Biophys J 92:2451–2462