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## THE POSSIBLE MECHANISMS OF THE DEVELOPMENT OF TOXICITY OF LOCAL AMINOAMIDE ANESTHETICS: LIPID-MEDIATED ACTION OF ROPIVACAINE

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The work is devoted to the identification of the molecular mechanisms of action of local anesthetic ropivacaine and other aminoamides, mepivacaine and bupivacaine, on the physicochemical properties of the membranes: the boundary potential and its components, the permeability for fluorescent marker, the temperature and cooperativity of the main transition of membrane forming lipids and mosaic organization of the bilayer; and also the processes of the formation and functioning of ion channels of the various nature in the planar lipid bilayers. It was found that ropivacaine, mepivacaine and bupivacaine, increased the membrane boundary potential mainly due to a change in the surface charge of the bilayer. It was demonstrated that the permeability of lipid vesicles for calcein increased with

the introduction of aminoamides, while the temperature and cooperativity of saturated phosphocholines decreased. The effect of the anesthetics on the packing density of the lipids in the membrane depended on the hydrophobicity of their molecules. A comparison of the effects of aminoamides on the functioning of different ion channels allowed to identify three mechanisms action of aminoamides anesthetics: by the increasing the surface potential of the membrane, decreasing the packing density of lipids in the membrane and blocking ion channels.

**Keywords:** local anesthetics, membranes, liposomes, ion channels, membrane dipole potential, spontaneous curvature, fluidity, heterogeneity