The Local Anesthetic Proparacaine Modifies Sodium Transport in Toad Skin and Perturbs the Structures of Model and Cell Membranes

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Experimental results indicate a significant decrease in the potential difference (PD) and in the short-circuit current (Isc) after the application of proparacaine to isolated toad skin, which may reflect an inhibition of the active transport of ions. This finding was explained on the basis of the results obtained from membrane models incubated with proparacaine. These consisted of human erythrocytes, isolated unsealed human erythrocyte membranes (IUM), phospholipid multilayers built-up of dimyristoylphosphatidylcholine (DMPC) and dimyristoylphosphatidylethanolamine (DMPE), representatives of phospholipid classes located in the outer and inner monolayers of the human erythrocyte membrane, respectively, and in large unilamellar vesicles (LUV) of DMPC. X-ray diffraction showed that proparacaine interaction with DMPC and DMPE bilayers perturbed both structures, especially DMPC. This result, confirmed by fluorescence spectroscopy of DMPC LUV at 18 °C, demonstrated that the local anesthetic (LA) could interact with the lipid moiety of cell membranes. However, effects observed by scanning electron microscopy (SEM) of human erythrocytes and by fluorescence spectroscopy of IUM might also imply proparacaine-protein interactions. Thus, the LA may alter epithelial sodium channels through interaction with the lipid matrix and with channel protein residues.