Effect of Cholesterol on the Bending Modulus of Membranes and the Electroporation Induced Pore Formation of Vesicles

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Abstract

The effects of cholesterol (chol, C_h) in the membranes of giant unilamellar vesicles (GUVs) on the size distribution of vesicles and the irreversible electroporation (IRE)-induced pore formation in GUVs were investigated. Dioleoylphosphatidylcholine (DOPC) /chol-GUVs and dioleoylphosphatidylglycerol (DOPG)/DOPC/chol-GUVs were prepared using the natural swelling method. The average sizes of GUVs were obtained from the size distribution histograms of vesicles which was fitted by the lognormal distribution. The size of GUVs increased with the increase of C_h in neutral and charged membranes. Using the theorical approach, the values of bending modulus (K_{ben}) were obtained 19.1 ± 0.1, 23.1 ± 0.1, 28.6 ± 0.01 and 31.0 ± 0.1 k_BT (here k_B is the Boltzmann constant and T is absolute temperature) for DOPC/chol (100/0), DOPC/chol (85/15), DOPC/chol (71/29) and DOPC/chol (60/40)-GUVs, respectively. The values of K_{ben} were also increased with C_h for charged membrane. Irreversible electroporation (IRE) signal (pulsating direct current) induced lateral electric tension in the membranes of GUVs. The time dependent fraction of intact GUVs among all the examined GUVs was fitted to a single exponential decay function from where the rate constant (k_p) of pore formation was obtained. The values of k_p were obtained $(1.0 \pm 0.1)\times10^{-2}$ s^{-1} at 7.0 mN/m, $(2.9 \pm 0.3)\times10^{-2}$ s^{-1} at 8.0 mN/m, $(11.0 \pm 0.3)\times10^{-2}$ s^{-1} at 9.0 mN/m for DOPG/DOPC/chol (46/39/15)-GUVs, respectively. The similar increase of k_p was also obtained for other C_h content. The estimated line tension increased from 12.9 to 14.6 pN with the increase of C_h from 15 to 40 mole%. The increased energy barrier in the prepore state, due to the increase of C_h, was the main factor for decreasing the k_p. Hence, the increase of K_{ben} due to C_h controlled the k_p of IRE-induced pore formation in GUVs.