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Effects of t-Butyl Hydrogen Peroxide on the Maxi-K Channels of Rat Brain

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Oxidation and reduction of amino acid residues in proteins affect their functional properties. Especially, redox modulation of ion channel activities has been reported in number of ion channel proteins. In this study, we investigated the effects of tertiary-butyl hydrogen peroxide (tBHP) on the large-conductance Ca^{2+}-activated K^+ (Maxi-K) channel of rat brain using lipid bilayer reconstitution technique.

When tBHP was applied to the cis solution, the open probability (P_o) increased within 1 min in dose-dependent manner (n=21). The degree of tBHP effects was diverse between experiments. However, there was a correlation between the per cent changes in P_o and the P_o before tBHP application (P_{init}). Namely, the P_o increased more when the P_{init} was lower, but remained relatively unchanged when the P_{init} was over 0.5. tBHP effects did not reverse immediately, suggesting tBHP induces some chemical modification on the channel protein. From kinetic analysis of single channel data (n=3), the increase in the Po appears to be mainly due to shortening of closed dwell time.

Redox modulation of Maxi-K channels by various agents has been reported, where the oxidants such as diamide, thimerosal, and GSSG decreased the activities of Maxi-K channel. One of possible explanations is a difference in target residues on Maxi-K channels between oxidants. The oxidants in previous experiments mainly target cystein residues with disulfide bond while tBHP modifies methionine residues into a sulfoxide form. Different oxidation pattern might produce different effects. Further studies are needed to explain various effects by oxidation and reduction of Maxi-K channel protein at molecular level.