

Lithspermic acid-A slows down the inactivation kinetics of cardiac Na⁺ current by intracellular Ca²⁺-dependent mechanismsJin-Young Yoon¹, Hyuncheol Oh², Won-Kyung Ho¹, and Suk-Ho Lee¹¹Department of Physiology, Seoul National University College of Medicine
and 28 Yonkeun-Dong, Seoul, 110-799, Korea²Medicinal Resources Research Center of Wonkwang University, Iksan, Chonbug,
570-749*.

Salviae Miltiorrhizae Radix has been used for treatment of cardiovascular diseases in oriental medicine. To investigate the possible involvement of cardiac ion channel in this effect, we examined electrophysiological effects of the extract of *Salviae Miltiorrhizae Radix* on action potentials and ionic currents in rat ventricular myocytes. The extracts of *Salviae Miltiorrhizae Radix* were fractionated into nine fractions, and the effect of each fraction on action potential was tested. The fraction containing monomethyl lithospermic acid-A (LSA-A) induced a significant prolongation of action potential duration (APD). LSA-B which is a major component of *Salviae Miltiorrhizae Radix*, however, did not cause a significant effect. In voltage clamp experiments, the effects of LSA-A on K currents, Ca currents and Na currents were tested. Neither K currents nor L-type Ca currents were affected by LSA-A. On the contrary, LSA-A significantly slowed down the inactivation kinetics of the Na current with no effect on the fast component of the inactivation process. The amplitude of the peak current and the voltage-dependence of activation were not changed by LSA-A. The effect of LSA-A on Na current was abolished when high concentration of Ca²⁺ buffer (10 mM BAPTA) was included in the pipette solution or when Ca²⁺ current was blocked by nifedipine (1 μM) in the bath solution.

From these results, it was suggested that LSA-A causes APD prolongation in ventricular myocytes by slowing inactivation mechanism of Na channels, and this effect was dependent on intracellular Ca²⁺.

Acknowledgment

This study was supported by the grant from the Ministry of Health and Welfare (HMP-00-CO-03-0003).