EFFECTS OF NIFEDIPINE AND BAY K 8644 ON CONTRACTILE ACTIVITIES IN SINGLE SKELETAL MUSCLE FIBERS OF THE FROG

Naoki Kitamura
Department of Pharmacology, Faculty of Veterinary Medicine, Hokkaido University, Sapporo 060, Japan

1. The effects of the dihydropyridine derivatives, nifedipine and Bay K 8644 on twitch responses and K⁺ contractures of single fibers of frog skeletal muscles were examined in the presence and absence of extracellular Ca²⁺. The effects of dihydropyridine derivatives on Ca²⁺-induced contraction in skinned fiber preparations were also examined.

2. Nifedipine (< 100 μM) in the presence of Ca²⁺, and low concentrations of nifedipine in the absence of Ca²⁺, enhanced twitch responses. Bay K 8644 at low concentrations (< 30 μM) enhanced twitch responses regardless of the presence or absence of Ca²⁺. However, high concentrations of nifedipine in the absence of Ca²⁺ and Bay K 8644 abolished twitch responses by inhibition of action potentials both in the presence and absence of Ca²⁺.

3. Twitch responses enhanced by Bay K 8644, but not by nifedipine, were partially inhibited by adenine, suggesting the involvement of Ca²⁺-induced Ca²⁺ release from sarcoplasmic reticulum in the potentiating response to Bay K 8644.

4. Neither nifedipine nor Bay K 8644 at 10 μM, which caused potentiation of twitch responses, affected Ca²⁺-induced contraction (pCa 5.5) in skinned fibers.

5. Both nifedipine and Bay K 8644 caused a dose-dependent potentiation of peak amplitudes of K⁺ contractures and accelerated inactivation without any effects on the membrane potentials in the presence of Ca²⁺. Conversely, both dihydropyridine derivatives inhibited K⁺ contractures in the absence of Ca²⁺.

6. These results suggest that dihydropyridine derivatives modify contractile activities of skeletal muscles by modulating the function of the dihydropyridine receptor acting as a voltage sensor. They also suggest that dihydropyridine derivatives accelerate activation and inactivation of the voltage sensor, inactivation of which is enhanced by the reduction of extracellular Ca²⁺.