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The role of L-type Calcium Channels in ureter smooth muscle action potential and its modulation by Nifedipine

Chitaranjan Mahapatra, Rohit Manchanda

Department of Bio Sciences & Bio Engineering, Indian Institute of Technology Bombay, India

Objectives: Adequate abnormalities to kidney and upper urinary tract are strongly associated with renal failure. Abnormal peristaltic contraction of the ureter smooth muscle (USM) causes pathophysiological condition to the urinary system. It is demonstrated that the USM contractions are discretely initiated by the USM cell action potentials (APs). L- type calcium channels (LTCCs) are prevalent in different systems and hold immense importance for maintaining/performing selective functions. The present study investigates the role of LTCCs in modulating the USM cell APs.

Methods: The USM cell is described as an equivalent electrical circuit with a number of variable conductances representing two voltage-gated Ca^{2+} (T - type and L- type) channels, one voltage-gated fast potassium channels, one calcium-dependent large conductance potassium channels, and HCN channel. A drug model for the LTCC blocker nifedipine is simulated by multiplying the maximal conductance of LTCC with a scaling factor between 0 and 1 to mimic the drug concentration.

Results: The resting membrane potential (RMP) of the USM is set at -52mV . The peak amplitude of the AP and total inward current are substantially reduced after adding nifedipine by 50% (black solid line) and 100% (blue solid line) of its control value (red solid line) in Figure 1. The results show that LTCC plays important role in generating APs and it is the major contributor to the total inward current. The experimental USM cell APs show a large variation in terms of AP duration. It is also observed that the inactivation time constant of the L -type Ca^{2+} channels regulate the repolarization phase and duration of the AP.

Conclusions: The L-type Ca^{2+} channel blocker can be used as a new pharmacological target for abnormal ureter contraction. The other specific roles L-type Ca^{2+} channel in cellular signaling can also be investigated by future studies.

Figure 1. AP modulation by Nifedipine

