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Chelidonine blocks hKv1.5 channel current

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Voltage-gated K^+ (Kv) channels represent a structurally and functionally diverse group of membrane proteins. These channels play an important role in determining the length of the cardiac action potential and are the targets for antiarrhythmic drugs. Many K^+ channel genes have been cloned from human myocardium and functionally contribute to its electrical activity. One of these channels, Kv1.5, is one of the more cardiovascular-specific K^+ channel isoforms identified to date and forms the molecular basis for an ultra-rapid delayed rectifier K^+ current found in human atrium. Thus, the blocker of hKv1.5 is expected to be an ideal antiarrhythmic drug for atrial fibrillation. Chelidonine was isolated from *Chelidonium majus* L. We examined the effect of chelidonine on the hKv1.5 current expressed in Ltk-cells using whole cell mode of patch clamp techniques. Chelidonine selectively inhibited the hKv1.5 current expressed in Ltk-cells in a concentration-dependent manner, whereas did not affect the HERG current expressed in HEK-293 cells. Additionally, chelidonine reduced the tail current amplitude recorded at -50 mV after 250 ms depolarizing pulses to +60 mV, and slowed the deactivation time course resulting in a 'crossover' phenomenon when the tail currents recorded under control conditions and in the presence of chelidonine were superimposed. We found that chelidonine also inhibited the K^+ current in isolated human atrial myocytes where hKv1.5 channels were predominantly expressed. Furthermore, we examined the effects of chelidonine on the action potentials in rabbit hearts using conventional microelectrode technique. Chelidonine prolonged the action potential durations (APD) of atrial, ventricular myocytes and Purkinje fibers in a dose-dependent manner. However, the effect of chelidonine on atrial APD was frequency-dependent whereas the effect of chelidonine on the APDs of ventricular myocytes and Purkinje fibers was not frequency- dependent. Also, the selective action of chelidonine on heart was more potent than dofetilide, K^+ channel blocker.