

➤ Background

Increased Action Potential duration (APD) is associated with prolongation of the QT interval and can lead to a serious ventricular arrhythmia, torsade de pointes. In rabbit Purkinje fibers action potential waveform, underlying ionic currents and ion channel pharmacological properties are similar to those of humans. This action potential assay on Purkinje Fibers allows wide-ranging adjustment of stimulation rate and drug concentration so intracellular recordings in Purkinje fibers are an important component of nonclinical testing for drug-induced action potential prolongation.

➤ Action Potential Assay specifics

- Compound profiling against the action potential in rabbit Purkinje fibers to evaluate potential cardiac liability
- Two microelectrode intracellular recording with the chamber temperature of 36°C
- Three frequency stimuli were used to test the use-dependent effect of compound
- Positive control and vehicle control in every assay
- Three concentration profiling with 12 pt. ; n=4.

➤ Reverse use-dependence of Dofetilide prolonging AP in Purkinje fiber

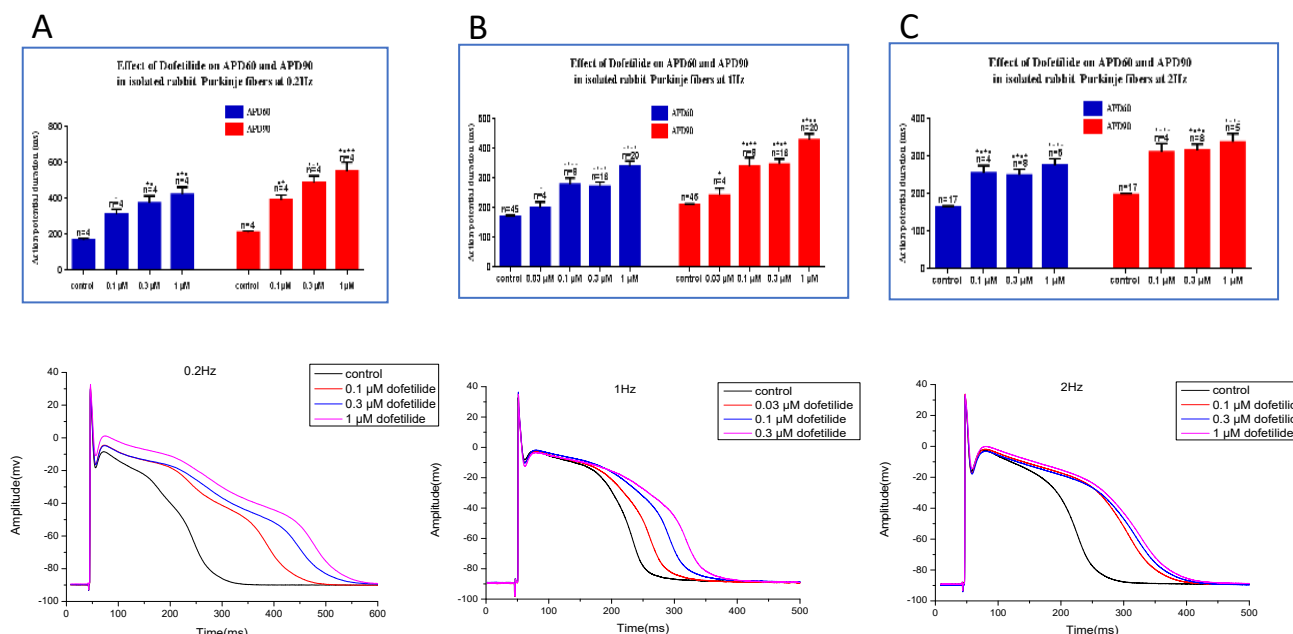


Figure 1. The effects of dofetilide on action potential duration prolongation with use-dependency. Action potentials were elicited by the stimuli of 0.2, 1, and 2 Hz in the presence of dofetilide from 0.1, 0.3, and 1 μM. Upper panels of A, B, and C show the summary of action potential prolongation by dofetilide and the lower panel shows the action potential traces.