

ACTION POTENTIAL KINECTICS (APD)

Assay

Action Potential Kinectics analysis in Purkinje fibres or contractile cardiac tissue

Tissues & species

Ventricular strips, trabeculae, papillary muscle, Purkinje fibres or cardiomyocytes
Species : guinea-pig, rabbit, dog, & human

Technique

High-resistance micro-electrode impalement

GLP Compliance

Pre-IND (GLP-compliant) or exploratory designs (non-GLP compliant)

Rationale

The cardiac action potential (AP) is the sum of over 15 ionic currents, most of which can be altered in the event of QT interval prolongation. This test verifies the direct interaction of a test article with all the channels involved in AP generation, and can point to the exact population of channels affected in the event of AP elongation. The APD assay is also useful in quantifying relevant characteristics such as rate-dependence and pathological effects such as hypokalemia, hypothermia, etc. In addition, it is a robust system favourable to the generation of electrical adverse events such as delayed or early after-depolarizations.

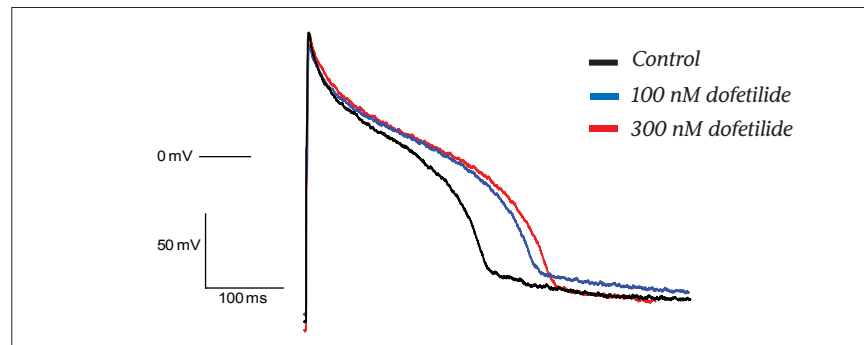


Figure 1. Effect of dofetilide on action potentials in canine Purkinje fibres.

Protocol outline

Number of tissues analyzed : 5 (screen : 3)
Number of concentrations of the test article : 4 (screen : 3)
Method of test article exposure : Continuous perfusion
Stimulation frequencies : 0.3, 1.0, 3.0 Hz
Positive controls commonly used : E-4031, dofetilide, d,l-sotalol, or terfenadine

Study outcome

- A quantitative assessment of multiple-channel interactions with 4 concentrations of the test article assessed at one or more frequencies
- Determination of the IC50 value (if applicable) on APD30, APD60, and APD90
- FDA-ready hard-copy and e-report for electronic IND submission
- Holistic interpretation of all signals, considering other existing pre-clinical data

Recommended readings

1. Jalaie M, Holsworth DD. QT interval prolongation: and the beat goes on., *Mini Rev Med Chem* 5(12):1083-91, Dec;5(12):1083-91, 2005.
2. Antzelevitch C, Oliva A. Amplification of spatial dispersion of repolarization underlies sudden cardiac death associated with catecholaminergic polymorphic VT, long QT, short QT and Brugada syndromes., *J Intern Med.*, 259(1):48-58, 2006.

Contact us:

info@ipstherapeutique.com

(P) 819.564.5391

(F) 819.820.6831