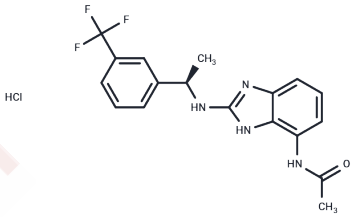
Data Sheet (Cat.No.T39963)

TargetMol

AP14145 hydrochloride

Chemical Properties



CAS No. : 2387505-59-9

Formula: C18H18ClF3N4O

Molecular Weight: 398.81

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	AP14145 hydrochloride is a potent negative allosteric modulator of K Ca 2 (SK) channels, specifically targeting K Ca 2.2 (SK2) and K Ca 2.3 (SK3) channels with an IC 50 of 1.1 μM. Inhibition of AP14145 hydrochloride is highly influenced by S508 and A533 amino acids present in the channel. This compound effectively extends the atrial effective refractory period (AERP) in rats and exhibits antiarrhythmic properties in a Vernakalant-resistant porcine model of atrial fibrillation (AF).
Targets(IC50)	Others,Potassium Channel
In vitro	AP14145, at concentrations ranging from 10 nM to 30 μM, effectively inhibits the currents of hKCa2.2 and hKCa2.3 channels in a concentration-dependent manner. At a concentration of 10 μM, AP14145 inhibits 50% of the hKCa1.1 current and 90% of the hKCa2.1 current, while it does not affect hKCa3.1 channels. Additionally, at 10 μM, it increases the EC50 of Ca2+ on KCa2.3 channels from 0.36 to 1.2 μM. AP14145 hydrochloride exhibits an IC50 of 1.3 μM against the human SK3 channel in whole-cell patch clamp assays, inhibits hERG (KV11.1) with an IC50 of 71.8 μM, and Kir3.1/Kir3.4 (IKACh) with an IC50 of 9.3 μM. It has no significant effect on KV1.5 (IKur), KV7.1/KCNE1 (IKs), KV4.3/KChiP2 (Ito), and Kir2.1 (IK1) at 30 μM or on NaV1.5 (15 μM; INa) across a panel of cardiac ion channels. At concentrations between 1-10 μM, AP14145 does not significantly block CaV1.2 channels.
In vivo	AP14145 at 10 μM extends the atrial effective refractory period (AERP) in isolated perfused rat hearts, demonstrating comparable effects with bolus intravenous injections of 2.5 and 5 mg/kg in male Sprague-Dawley rats (weighing 250-350 g and aged 1-3 months)[1]. Additionally, a dosage of 5 mg/kg in Landrace pigs (12-13 weeks old, weighing 30-35 kg) results in a maximum concentration (C max) of 8355 nmol/L and a half-life (t½) of 24.3 minutes[2].

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5075 mL	12.5373 mL	25.0746 mL
5 mM	0.5015 mL	2.5075 mL	5.0149 mL
10 mM	0.2507 mL	1.2537 mL	2.5075 mL
50 mM	0.0501 mL	0.2507 mL	0.5015 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Rafel Simó-Vicens, et al. A New Negative Allosteric Modulator, AP14145, for the Study of Small Conductance Calcium-Activated Potassium (K Ca 2) Channels. Br J Pharmacol. 2017 Dec;174(23):4396-4408.
Jonas Goldin Diness, et al. Termination of Vernakalant-Resistant Atrial Fibrillation by Inhibition of Small-Conductance Ca 2+ -Activated K + Channels in Pigs. Circ Arrhythm Electrophysiol. 2017 Oct;10(10):e005125.