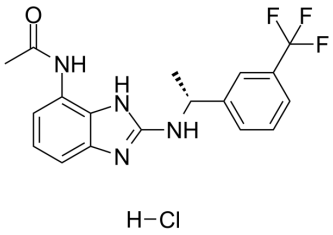
AP14145 hydrochloride

Cat. No.:	HY-120355A
CAS No.:	2387505-59-9
Molecular Formula:	$C_{18}H_{18}ClF_3N_4O$
Molecular Weight:	398.81
Target:	Potassium Channel
Pathway:	Membrane Transporter/Ion Channel
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	AP14145 hydrochloride is a potent $K_{Ca}2$ (SK) channel negative allosteric modulator with an IC_{50} of 1.1 μM for $K_{Ca}2.2$ (SK2) and $K_{Ca}2.3$ (SK3) channels. AP14145 hydrochloride inhibition strongly depends on two amino acids, S508 and A533 in the channel. AP14145 hydrochloride prolonged atrial effective refractory period (AERP) in rats and demonstrates antiarrhythmic effects in a Vernakalant-resistant porcine model of atrial fibrillation (AF)[1][2].
IC_{50} & Target	IC50: 1.1 μM ($K_{Ca}2.2$) and 1.1 μM ($K_{Ca}2.3$)[1]
In Vitro	AP14145 (10 nM-30 μM) inhibits both h$K_{Ca}2.2$ and h$K_{Ca}2.3$ channel currents in a concentration⊠dependent fashion. AP14145 (10 μM) inhibits 50% of the h$K_{Ca}1.1$ current, 90% of the h$K_{Ca}2.1$ current and has no effect on h$K_{Ca}3.1$ channel. AP14145 (10 μM) increases the EC_{50} of Ca^{2+} on $K_{Ca}2.3$ channels from 0.36 to 1.2 μM[1]. AP14145 hydrochloride demonstrates an IC_{50} in whole-cell patch clamp on the human SK3 channel of 1.3 μM. AP14145 inhibits hERG ($K_V11.1$) with an IC_{50} of 71.8 μM and $K_{ir}3.1/K_{ir}3.4$ (I_{KACh}) with an IC_{50} of 9.3 μM and does not produce any significant effects on $K_V1.5$ (I_{Kur}), $K_V7.1$/KCNE1 (I_{Ks}), $K_V4.3$/KChiP2 (I_{to}), and $K_{ir}2.1$ (I_{K1}) in 30 μM or on $Na_V1.5$ (15 μM; I_{Na}) on a panel of cardiac ion channels. AP14145 (1-10 μM) produces no significant block of $Ca_V1.2$[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AP14145 (10 μM) increases the duration of the atrial effective refractory period (AERP) in isolated perfused rat hearts[1]. AP14145 (2.5 and 5 mg/kg; bolus injections (iv)) increases the duration of the atrial effective refractory period in male sprague-dawley rats (250-350 g, 1-3 months old)[1]. AP14145 (5 mg/kg; bolus injections) has a C_{max} of 8355 nmol/L, a $t_{½}$ of 24.3 minutes in landrace pigs (12-13 weeks old, 30-35 kg gilts)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. 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.

[2]. 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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