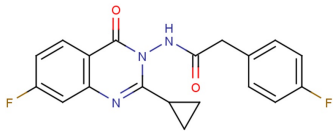
Data Sheet (Cat.No.T11606)

TargetMol
A DRUG SCREENING EXPERT

ICA-105665

Chemical Properties



CAS No.:	T11606
Formula:	C19H15F2N3O2
Molecular Weight:	355.34
Appearance:	N/A
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	ICA-105665 is a potent and orally active neuronal Kv7.2/7.3 and Kv7.3/7.5 potassium channels opener. It can penetrate the blood-brain barrier and has antiseizure effects. ICA-105665 inhibits liver mitochondrial function and bile salt export protein (BSEP) transport (IC50: 311 μM).
Targets(IC_{50})	Kv7.2/7.3 and Kv7.3/7.5 potassium channels: None
In vitro	The mitochondrial respiratory reserve is compromised in human hepatocytes treated with ICA-105665 (PF-04895162) at concentrations >11 μM for 25 minutes. ICA-105665 does not display potent cytotoxic properties in THLE and HepG2 cell lines (IC50 ~192 μM and 130 μM after 72 hours, respectively) or in human hepatocytes (AC50 for cell loss at 48 hours was >125 μM based on results in three assessments in two different human hepatocyte lots (LBN and HU4165) [1].
In vivo	ICA-105665 has demonstrated broad-spectrum antiseizure activity in multiple animal models including maximal electroshock, 6 Hz seizures, pentylenetetrazole, and electrical kindling at doses from <1 to 5 mg/kg [3]. For ICA-105665, in a 7-day rat toxicity study, dose-dependent alanine aminotransferase (ALT) elevations, potentially indicative of liver toxicity, were observed. However, no histological evidence of liver injury was identified, and ALT elevations were not confirmed in a repeat 7-day study. Further, 28 day and 6-month toxicity studies in rats were negative for transaminase elevations and liver toxicity, and toxicity studies up to 9 months duration in cynomolgus monkeys were also negative [2].

Solubility Information

Solubility	< 1 mg/ml refers to the product slightly soluble or insoluble

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.814 mL	14.071 mL	28.142 mL
5 mM	0.563 mL	2.814 mL	5.628 mL
10 mM	0.281 mL	1.407 mL	2.814 mL
50 mM	0.056 mL	0.281 mL	0.563 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. Aleo MD, et al. Phase I study of PF-04895162, a Kv7 channel opener, reveals unexpected hepatotoxicity in healthy subjects, but not rats or monkeys: clinical evidence of disrupted bile acid homeostasis. Pharmacol Res Perspect. 2019 Feb;7(1):e00467.
2. Generaux G, et al. Quantitative systems toxicology (QST) reproduces species differences in PF-04895162 liver safety due to combined mitochondrial and bile acid toxicity. Pharmacol Res Perspect. 2019 Oct 9;7(6):e00523.
3. Kasteleijn-Nolst Trenité DG, et al. Kv7 potassium channel activation with ICA-105665 reduces photoparoxysmal EEG responses in patients with epilepsy. Epilepsia. 2013 Aug;54(8):1437-43.
4. Bialer M, et al. Progress report on new antiepileptic drugs: a summary of the Eleventh Eilat Conference (EILAT XI). Epilepsy Res. 2013 Jan;103(1):2-30.

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