ICA-105665

Cat. No.: HY-125469

CAS No.: 2694728-63-5

Molecular Formula: $C_{19}H_{15}F_2N_3O_2$

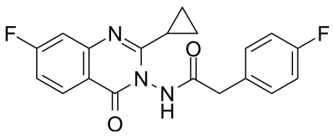
Molecular Weight: 355.34

Target: Potassium Channel

Pathway: Membrane Transporter/Ion Channel

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (703.55 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8142 mL	14.0710 mL	28.1421 mL
	5 mM	0.5628 mL	2.8142 mL	5.6284 mL
	10 mM	0.2814 mL	1.4071 mL	2.8142 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

ICA-105665 (PF-04895162) is a potent and orally active neuronal Kv7.2/7.3 and Kv7.3/7.5 potassium channels opener. ICA-105665 inhibits liver mitochondrial function and bile salt export protein (BSEP) transport (IC_{50} of 311 μM). ICA-105665 can penetrate the blood-brain barrier and has antiseizure effects[1][2][3][4].

IC_{50} & Target

Kv7.2/7.3 and Kv7.3/7.5 potassium channels[1][2]

In Vitro

ICA-105665 (PF-04895162) does not display potent cytotoxic properties in THLE and HepG2 cell lines (IC_{50} ~192 μM and 130 μM after 72 hours, respectively) or in human hepatocytes (AC_{50} 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].

Mitochondrial respiratory reserve is compromised in human hepatocytes treated with ICA-105665 (PF-04895162) at concentrations >11 μM for 25 minutes[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

For ICA-105665 (PF-04895162), 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].

ICA-105665 (PF-04895162) 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[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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