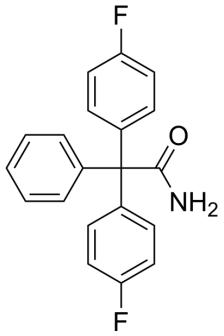
Senicapoc



Cat. No.:	HY-50694
CAS No.:	289656-45-7
Molecular Formula:	$C_{20}H_{15}F_2NO$
Molecular Weight:	323.34
Target:	Potassium Channel
Pathway:	Membrane Transporter/Ion Channel
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year

SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (154.64 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0927 mL	15.4636 mL	30.9272 mL
	5 mM	0.6185 mL	3.0927 mL	6.1854 mL
	10 mM	0.3093 mL	1.5464 mL	3.0927 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.73 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.73 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.73 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.5 mg/mL (7.73 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Senicapoc (ICA-17043) is a potent and selective Gardos channel (Ca^{2+}-activated K^+ channel; KCa3.1) blocker with an IC_{50} of 11 nM. Senicapoc blocks Ca^{2+}-induced rubidium flux from human RBCs with an IC_{50} value of 11 nM and inhibits RBC dehydration with IC_{50} of 30 nM[1].

IC_{50} & Target

IC50: 11 nM (Gardos channel)[1]

In Vitro	ICA-17043 is shown to block the Gardos channel of mouse (C57 Black) RBCs with an IC_{50} of 50±6 nM. ICA-17043 blocks this increase in cellular hemoglobin concentration in human RBCs in a concentration-dependent fashion[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ICA-17043?(10 mg/kg, p.o.) administration produces a significant decrease in Gardos channel activity measured at day 11 and 21 and is associated with a corresponding increase in red cell K^+ content without changes in Na^+ content. ICA-17043 (10 mg/kg, twice a day) induces a significant increase in Hct after 11 days of dosing in the SAD mouse[1]. Senicapoc (30 mg/kg, p.o.) reduces airway hyperresponsiveness, eosinophil numbers in bronchoalveolar lavage taken 48 hours post-allergen challenge, and vascular remodelling in the sheep[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The whole blood is initially diluted 1:1 with Modified Flux Buffer (MFB), consisting of 140 mM NaCl, 5 mM KCl, 10 mM Tris (tris(hydroxymethyl)aminomethane), 0.1 mM EGTA (ethyleneglycoltetraacetic acid) (pH=7.4). The blood is centrifuged at 1000 rpm, and the pellet comprised primarily of RBCs is washed 3 times with MFB. The cells are then loaded with $^{86}Rb^+$ by incubating the washed cells with $^{86}Rb^+$ at a final concentration of 0.185 MBq/mL (5 µCi/mL) in MFB for at least 3 hours at 37°C. After loading with $^{86}Rb^+$, the RBCs are washed 3 times with chilled MFB. The cells are then incubated for 10 minutes with test compound (senicapoc) at concentrations that ranged from 1 nM to 10 000 nM. Efflux of $^{86}Rb^+$ is initiated by raising intracellular calcium levels in the RBCs with the addition of $CaCl_2$ and A23187 (a calcium ionophore) to final concentrations of 2 mM and 5 µM, respectively. After 10 minutes of incubation at room temperature, the RBCs are pelleted in a microcentrifuge, and the supernatant is removed and counted in a Wallac MicroBeta liquid scintillation counter. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Transgenic Hbbsingle/single SAD1 (SAD) female and male mice between 3 and 6 months of age, weighing 25 to 30 g, are used for this study. The SAD mice are divided into 2 groups, and either vehicle (n=6) or senicapoc (10 mg/kg) (n=6) is administered orally by gavage twice daily. C57B6/2J mice are used as controls (wild-type mice). Hematologic parameters are evaluated at baseline and after 11 and 21 days of therapy. Blood sampling and vehicle administration have previously been shown not to affect the blood parameters measured in this study. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Haematologica. 2020 Mar;105(3):610-622.
- Haematologica. 2017 Oct;102(10):e415-e418.
- JCI Insight. 2019 Feb 21;4(4). pii: 126444.
- J Virol. 2019 Mar 5;93(6):e01744-18.
- Eur J Pharmacol. 2017 Jan 15;795:1-7.

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REFERENCES

[1]. Stocker JW, et al. ICA-17043, a novel Gardos channel blocker, prevents sickled red blood cell dehydration in vitro and in vivo in SAD mice. Blood. 2003 Mar 15;101(6):2412-8.

[2]. Van Der Velden J, et al. K(Ca)3.1 channel-blockade attenuates airway pathophysiology in a sheep model of chronic asthma. PLoS One. 2013 Jun 24;8(6):e66886.

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

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