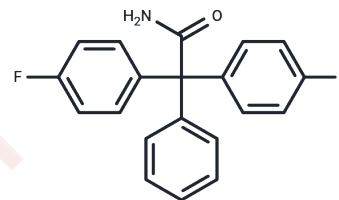


Senicapoc

Chemical Properties

CAS No. :	289656-45-7
Formula:	C ₂₀ H ₁₅ F ₂ NO
Molecular Weight:	323.34
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	Senicapoc (ICA-17043) is a potent inhibitor of the Gardos channel that ameliorates RBC dehydration in the SAD mouse. It blocks Ca ²⁺ -induced rubidium flux from human RBCs with an IC ₅₀ value of 11 ± 2 nM (CLT IC ₅₀ = 100 ± 12 nM) and inhibits RBC dehydration with an IC ₅₀ of 30 ± 20 nM. Senicapoc is used in the treatment of Sickle Cell Disease and Sickle Cell Anemia.
Targets(IC ₅₀)	Potassium Channel
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].
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].
Cell Research	Senicapoc is dissolved in DMSO or 100% ethanol. 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 ⁷ 000 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.

Solubility Information

A DRUG SCREENING EXPERT

Solubility	DMSO: 50 mg/mL (154.64 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (6.19 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0619 mL	0.3093 mL	0.6185 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

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.

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