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产品名称：Senicapoc
产品别名：塞尼卡泊 ； ICA-17043

生物活性：

Description	Senicapoc (ICA-17043) is a potent and selective Gardos channel blocker with IC_{50} value of 11 nM. It 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.
IC_{50} & Target	IC50: 11 nM (Gardos channel)
In Vitro	ICA-17043 is shown to block the Gardos channel of mouse (C57 Black) RBCs with an IC50 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].

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (7.73 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.73 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (7.73 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (7.73 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (7.73 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.73 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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. [3]. Staal RG, et al. Inhibition of the potassium channel KCa3.1 by senicapoc reverses tactile allodynia in rats with peripheral nerve injury. Eur J Pharmacol. 2017 Jan 15;795:1-7.

实验参考：

Cell Assay	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. [1]
Animal Administration	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. [1]
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. [3]. Staal RG, et al. Inhibition of the potassium channel KCa3.1 by senicapoc reverses tactile allodynia in rats with peripheral nerve injury. Eur J Pharmacol. 2017 Jan 15;795:1-7.