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产品名称：ELN-441958
产品别名：ELN-441958

生物活性：

Description

ELN-441958 is a potent, neutral antagonist of B1 receptor, inhibits the binding of the B1 agonist ligand [3H]DAKD to IMR-90 cells with Ki of 0.26 nM. ELN-441958 is highly selective for B1 over B2 receptors, and >500/ 2000-fold selective for the B1 over μ/δ-opioid receptor. IC50 value: 0.26 nM (Ki) Target: B1 Receptor in vitro: ELN-441958 is a novel small molecule bradykinin B1 receptor antagonist, based on the inhibition of agonist-induced increases in intracellular calcium in native and recombinant cells. ELN-441958 does not inhibit the activation of the human bradykinin B2 receptor at concentrations up to 10 μM, showing that it is highly selective for B1 over B2 receptors. ELN-441958 also displays good selectivity for B1 over other receptors examined in a broad screening panel. It is >500-fold and >2000-fold selective for the B1 receptor over the human μ- and δ-opioid receptor, the most potent off-target activity identified. In IMR-90 cells expressing the native human B1 receptor, ELN-441958 produced a concentration-dependent antagonism of the DAKD-induced calcium mobilization with a KB of 0.12 nM. [1] in vivo: ELN-441958 is essentially completely absorbed and produces high plasma levels after oral administration in rhesus monkeys.ELN-441958 has a moderate clearance and volume of distribution in both species following i.v. administration, consistent with the high metabolic stability in rat, rhesus, and human microsomes. ELN-441958 has high oral exposure and moderate plasma half-lives in rats and rhesus monkeys. The oral availability of ELN441958 in rats was 57%. ELN-441958 dose-dependently reduced carrageenan-induced thermal hyperalgesia in a rhesus monkey tail-withdrawal model, with an ED50 3 mg/kg s.c. [1]

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**199.59 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9959 mL	9.9796 mL	19.9593 mL
	5 mM	0.3992 mL	1.9959 mL	3.9919 mL
	10 mM	0.1996 mL	0.9980 mL	1.9959 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 (4.99 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.99 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 (4.99 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.99 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 (4.99 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.99 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]. Hawkinson JE, et al. Pharmacological, pharmacokinetic, and primate analgesic efficacy profile of the novel bradykinin B1 Receptor antagonist ELN441958. J Pharmacol Exp Ther.2007 Aug;322(2):619-630.