上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：A-1165442
产品别名：A-1165442

生物活性：

Description	A-1165442 is a potent, competitive and orally available TRPV1 antagonist with an IC50 of 9 nM for human TRPV1.
IC_{50} & Target	IC50: 9 nM (human TRPV1)[1]
In Vitro	A-1165442 displays potent, competitive antagonism at recombinant human TRPV1 activated by capsaicin (IC50=9 nM) and incomplete blockade of acid-evoked response (62% block at 30 μM). A-1165442 possesses excellent selectivity (>100-fold) versus other members of the TRP family (TRPA1, TRPM8, TRPV2, TRPV3) and other receptors expressed in peripheral sensory neurons including P2X2/3, Cav2.2, Nav channels, and KCNQ2/3. A-1165442 shows minimal cross-reactivity upon evaluation (10 μM) in a broad screening panel (n=74, CEREP) of cell-surface receptors, ion channels, and enzymes[1].
In Vivo	A-1165442 exhibits excellent pharmacological selectivity, has a favorable pharmacokinetic profile, and demonstrates good efficacy against osteoarthritis pain in rodents. Oral administration of A-1165442 prevents capsaicin-induced nocifensive behaviors in rats, with an ED_{50} of 9.5 μmol/kg corresponding to plasma concentration of 420 ng/mL (970 nM). A single dose of A-1165442 produces a robust effect on grip force, with an ED_{50} of 35 μmol/kg measured 1 h postdosing. Repeated dosing of A-1165442 results in an increase in potency relative to acute analgesic efficacy. No significant changes in core body temperature is observed in conscious rats dosed with A-1165442 and this temperature-neutral profile is maintained in conscious dogs[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (231.56 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3156 mL	11.5778 mL	23.1557 mL
	5 mM	0.4631 mL	2.3156 mL	4.6311 mL
	10 mM	0.2316 mL	1.1578 mL	2.3156 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 (5.79 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (5.79 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% corn oil Solubility: ≥ 2.5 mg/mL (5.79 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.79 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]. Voight EA, et al. Discovery of (R)-1-(7-chloro-2,2-bis(fluoromethyl)chroman-4-yl)-3-(3-methylisoquinolin-5-yl)urea (A-1165442): a temperature-neutral transient receptor potential vanilloid-1 (TRPV1) antagonist with analgesic efficacy. J Med Chem. 2014 Sep 11;57(17):7412-24.

实验参考：

Animal Administration	Dogs: Male beagle dogs are instrumented with telemetry transmitters capable of monitoring core body temperature and then allowed to recover. Dosing is initiated at time zero, with dogs receiving a single oral dose of vehicle, compound 1 at (30 μmol/kg), or A-1165442 (100 μmol/kg); n=4−6 per group. Measurements are recorded every 5 min for the duration of the study, then averaged to 15 min and 1 h intervals. Temperature signals are transmitted as radio signals by each implanted transmitter to a receiver placed on the cage and interfaced with a desktop personal computer[1].
References	[1]. Voight EA, et al. Discovery of (R)-1-(7-chloro-2,2-bis(fluoromethyl)chroman-4-yl)-3-(3-methylisoquinolin-5-yl)urea (A-1165442): a temperature-neutral transient receptor potential vanilloid-1 (TRPV1) antagonist with analgesic efficacy. J Med Chem. 2014 Sep 11;57(17):7412-24.