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产品名称：司替戊醇
产品别名：Stiripentol ；斯利潘托 ；BCX2600

生物活性：

Description	Stiripentol (STP) is an anticonvulsant agent, which can inhibit N-demethylation of CLB to NCLB mediatated by CYP3A4 (noncompetitively) and CYP2C19 (competitively) with K_i of 1.59±0.07 and 0.516±0.065 μM and IC_{50} of 1.58 and 3.29 μM, respectively.
IC_{50} & Target	IC50: 1.58 μM (CYP3A4), 3.29 μM (CYP2C19)[1] Ki: 1.59±0.07μM (CYP3A4), 0.516±0.065 μM (CYP2C19)[1]
In Vitro	Stiripentol (STP) is an anticonvulsant agent, which can inhibit N-demethylation of CLB to N-desmethylclobazam (NCLB) mediated by CYP3A4 (noncompetitively) and CYP2C19 (competitively). The inhibition of CLB demethylation by Stiripentol (STP) is best described by a noncompetitive inhibition model with apparent Ki=1.6 μM for the cDNA-expressing CYP3A4 and by a competitive inhibition model with Ki=0.52 μM for the cDNA-expressing CYP2C19. Formation of OH-NCLB from NCLB by cDNA-expressing CYP2C19 is competitively inhibited by Stiripentol (STP) with a Ki=0.14 μM[1].
In Vivo	In mice treating with Stiripentol (STP) monotherapy, the difference between BT_1 (39.67±1.09°C) and BT_2(41.32±1.05°C) reaches statistical significance (t=3.097, p<0.05). The difference in BT_2 between Stiripentol (STP) monotherapy and CLB monotherapy is statistically significant (t=2.615, p<0.05). In mice treating with Stiripentol (STP)+CLB combination therapy, the difference between BT_1 (40.18±0.58°C) and BT_2 (43.03±0.49°C) reaches statistical significance (t=10.44, p<0.01)[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 150 mg/mL** (**640.23 mM;** Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.2682 mL	21.3411 mL	42.6821 mL
	5 mM	0.8536 mL	4.2682 mL	8.5364 mL
	10 mM	0.4268 mL	2.1341 mL	4.2682 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: ≥ 2.08 mg/mL (8.88 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (8.88 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (8.88 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (8.88 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (8.88 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (8.88 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Giraud C, et al. In vitro and in vivo inhibitory effect of stiripentol on clobazam metabolism.Drug Metab Dispos. 2006 Apr;34(4):608-11. Epub 2006 Jan 13. [2]. Cao D, et al. Efficacy of stiripentol in hyperthermia-induced seizures in a mouse model of Dravet syndrome. Epilepsia. 2012 Jul;53(7):1140-5.

实验参考：

Cell Assay	The inhibition constants (apparent K_i) of Stiripentol (STP) for CLB demethylation by CYP3A4 and CYP2C19 are determined using various concentrations of CLB (2, 10, 20, 40, 60, and 100 μM) with increasing concentrations of Stiripentol (STP) (0, 0.5, 1, 2, and 5 μM). Concerning NCLB hydroxylation by CYP2C19, the apparent K_i is similarly determined with different concentrations of NCLB (1.5, 4, 6, 8, 12, and 14 μM) and STP (0, 0.1, 0.5, 1, and 2 μM). IC_{50} values are determined by coincubation of the substrate at concentration in the range of the therapeutic plasma concentrations (2 μM CLB or 14 μM NCLB) with increasing concentrations of Stiripentol (STP) (0.001, 0.002, 0.005, 0.01, 0.05, 0.1, 0.25, 2, 5, and 10 μM)[1].
Animal Administration	Two age groups, p1M (n=18, age 4 weeks) and p5M (n=18, age 5-10 months), of *Scn1a*$^{RX/+}$ mice are assigned in this experiment. Both groups are divided randomly into three subgroups (n=6), and each subgroup is administered Stiripentol (STP) (300 mg/kg) alone, CLB (6.62 mg/kg) alone, or a combination of Stiripentol (STP) (p1M; 150 mg/kg, p5M; 300 mg/kg) and CLB (6.62 mg/kg). All drugs are administered by intraperitoneal injection (i.p.) after a 48-h recovery from baseline seizure study. Blood samples are collected at 1 h and 20 min after administration of CLB or STP+CLB for measurement of plasma concentrations of CLB and N-desmethylclobazam, respectively[2].
References	[1]. Giraud C, et al. In vitro and in vivo inhibitory effect of stiripentol on clobazam metabolism.Drug Metab Dispos. 2006 Apr;34(4):608-11. Epub 2006 Jan 13. [2]. Cao D, et al. Efficacy of stiripentol in hyperthermia-induced seizures in a mouse model of Dravet syndrome. Epilepsia. 2012 Jul;53(7):1140-5.