Stiripentol

Cat. No.: HY-103392

CAS No.: 49763-96-4

Molecular Formula: $C_{14}H_{18}O_3$

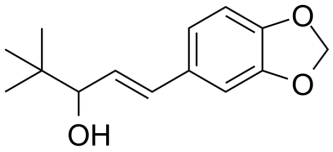
Molecular Weight: 234.29

Target: Cytochrome P450

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (8.88 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (8.88 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (8.88 mM); Clear solution

BIOLOGICAL ACTIVITY

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 K_i=1.6 μM for the cDNA-expressing CYP3A4 and by a competitive inhibition model with K_i=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 K_i=0.14 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

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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.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA