ELN-441958

Cat. No.: HY-15043

CAS No.: 913064-47-8

Molecular Formula: $C_{29}H_{29}ClN_4O_2$

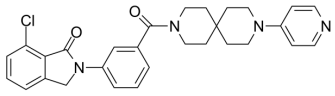
Molecular Weight: 501.02

Target: Bradykinin Receptor

Pathway: GPCR/G Protein

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 : 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

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: ≥ 2.5 mg/mL (4.99 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.99 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ELN-441958 is a potent, neutral, competitive and selective bradykinin B_1 receptor antagonist with a K_i of 0.26 nM against native human bradykinin B_1 receptor. ELN-441958 has high oral bioavailability, and has low CNS exposure in the mouse[1].

IC_{50} & Target

K_i: 0.26 nM (native human bradykinin B_1 receptor)[1]

In Vitro

ELN-441958 is selective for primate over rodent B_1 receptors with a rank order potency (K_B, nanomolar) of human (0.12 ± 0.02) ~ rhesus monkey (0.24 ± 0.01) > rat (1.5 ± 0.4) > mouse (14 ± 4)[1].

ELN-441958 has good permeability and metabolic stability[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

ELN-441958 (1-10 mg/kg; s.c.; once) dose-dependently reduces carrageenan-induced thermal hyperalgesia in a rhesus monkey tail-withdrawal model[1].

ELN-441958 (0-10 mg/kg; i.v. or p.o.) exhibits a favorable pharmacokinetic profile in the rat and rhesus monkey[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Adult male and female rhesus monkeys[1]
Dosage:	1, 3, or 10 mg/kg
Administration:	Subcutaneous injection, 30 min before carrageenan injection
Result:	Increased the tail-withdrawal latencies in a dose-dependent manner.

Animal Model:	Rhesus monkeys or Sprague-Dawley rats[1]
Dosage:	2.5 or 10 mg/kg for rats, 1 mg/kg or 5 mg/kg for rhesus monkeys
Administration:	Intravenous injection (2.5 mg/kg and 1 mg/kg) or oral administration (10 mg/kg and 5 mg/kg) (Pharmacokinetic Analysis)
Result:	In rats: When dosed intravenously, showed a moderate volume of distribution (2.7 L/kg, approximately four times total body water) and a moderate clearance (0.96 L/h/kg, approximately 24% of hepatic blood flow). The terminal plasma half-life of this compound in rats was 1.7 h. When dosed orally, the concentrations increased to a maximum of 1.2 g/mL at 2 h after dosing. The oral availability was 57%. In rhesus monkeys: When dosed intravenously, showed a moderate volume of distribution (2.7 L/kg) and a moderate clearance (0.49 L/h/kg, approximately 32% of hepatic blood flow). The terminal plasma half-life was 3.9 h. When dosed orally, the concentrations increased to a maximum of 3.6 g/mL at 3.3 h after dosing. The calculated oral bioavailability was greater than 100%.

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.

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