CI-1044

Cat. No.: HY-100246

CAS No.: 197894-84-1

Molecular Formula: $C_{23}H_{19}N_5O_2$

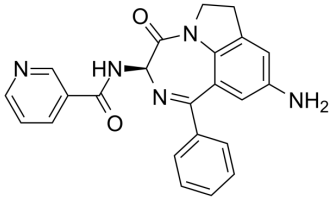
Molecular Weight: 397.43

Target: Phosphodiesterase (PDE)

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 : 100 mg/mL (251.62 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5162 mL	12.5808 mL	25.1617 mL
5 mM	0.5032 mL	2.5162 mL	5.0323 mL
10 mM	0.2516 mL	1.2581 mL	2.5162 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 (5.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.23 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CI-1044 is an orally active PDE4 inhibitor with IC_{50}s of 0.29, 0.08, 0.56, 0.09 μM for PDE4A5, PDE4B2, PDE4C2 and PDE4D3, respectively.

IC_{50} & Target

PDE4A5	PDE4B2	PDE4C2	PDE4D3
0.29 μM (IC_{50})	0.08 μM (IC_{50})	0.56 μM (IC_{50})	0.09 μM (IC_{50})

In Vitro

CI-1044 is an orally active PDE4 inhibitor with IC_{50}s of 0.29, 0.08, 0.56, 0.09 μM for PDE4A5, PDE4B2, PDE4C2 and PDE4D3, respectively. CI-1044 selectively inhibits PDE4 crude extract from U937 cells with an IC_{50} value of 0.27±0.02 μM being threefold more potent than rolipram (IC_{50}=0.91±0.14) and tenfold less potent than cilomilast (IC_{50}=0.026±0.007) in the same assay. In the presence of PDE4 inhibitors, the production of TNF-α is dose dependently decreased with mean IC_{50} values

	from three separate experiments of 0.31±0.05, 0.26±0.05 and 0.11±0.01 μM, for CI-1044, cilomilast and rolipram, respectively [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	TNF-α production is dose-dependently inhibited by CI-1044, rolipram and cilomilast with ID_{50}s of 0.4, 1.4 and 1.6 mg/kg respectively following single oral administration. Following repeated administration with CI-1044, the ID_{50} value represents 0.5 mg/kg p.o.. CI-1044 plasma levels increase proportionally with doses ranging between 0.1 and 40 mg/kg p.o. (R2=0.878). CI-1044 dose dependently inhibits the accumulation of eosinophils in Bronchoalveolar lavages (BAL) fluids with an ID_{50} value of 3.25 mg/kg. A single dose treatment with CI-1044 (10 mg/kg, p.o.) 24, 8, 3 or 1 h before the antigen challenge induces 6, 56, 48 and 79% inhibition in the number of eosinophils in BAL[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Blood from anesthetized rats is collected in heparin tubes, immediately distributed in 96-well microplates (250 μL/well) and incubated for 30 min at 37°C/5% CO_2. Twenty-five microliters of vehicle or increasing concentrations of CI-1044, rolipram, cilomilast or solvant (saline/DMSO<0.1%) are added in wells and incubated for 30 min before the addition of LPS (100 μ g/mL) or saline. Plasma is removed after a 22 to 24 h incubation at 37°C/5% CO_2, transferred in another 96-well microplate and stored at) -80°C until a TNF-α assay by ELISA[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Male rats (200 to 220 g) are used and receive either vehicle or CI-1044 orally at 0.4, 1, 4, 10 and 40 mg/kg. In the single administration experiment, all treatments are given 1 h before blood collection. In the repeated administration experiment, the treatments are given twice a day during 13 days and once on day 14, 1 h before blood sampling[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Pruniaux MP, et al. Relationship between phosphodiesterase type 4 inhibition and anti-inflammatory activity of CI-1044 in rat airways. Fundam Clin Pharmacol. 2010 Feb;24(1):73-82.

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