CI-1040

Cat. No.: HY-50295

CAS No.: 212631-79-3

Molecular Formula: $C_{17}H_{14}ClF_2IN_2O_2$

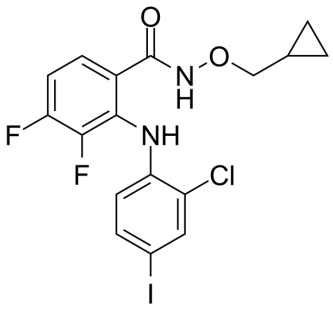
Molecular Weight: 478.66

Target: MEK; Apoptosis

Pathway: MAPK/ERK Pathway; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (208.92 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0892 mL	10.4458 mL	20.8917 mL
5 mM	0.4178 mL	2.0892 mL	4.1783 mL
10 mM	0.2089 mL	1.0446 mL	2.0892 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 (5.22 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CI-1040 (PD 184352) is an orally active, highly specific, small-molecule inhibitor of MEK with an IC_{50} of 17 nM for MEK1.

IC_{50} & Target

MEK1

17 nM (IC_{50})

In Vitro

CI-1040 directly inhibits MEK1 with an IC_{50} of 17 nM. It has also been shown to have little activity against a panel of related kinases with IC_{50} values more than 2.5 orders of magnitude higher. Treatment of whole cells with CI-1040 completely inhibits the mitogen-stimulated phosphorylation of ERK. CI-1040 at a concentration of 1 μM is found to inhibit phosphorylation of ERK1 and ERK2 by 99% and 92%, respectively in MDA-MB-231 breast cancer cells[1]. CI-1040 induces

	apoptosis and inhibits proliferation in U-937 cells in a dose and time-dependent manner. CI-1040 induces a significant increase in PUMA mRNA and protein levels[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The systemic administration of the MEK inhibitor CI-1040 reduces adenoma formation to a third and significantly restores lung structure. The proliferation rate of lung cells of mice treated with CL-1040 is decreased without any obvious effects on differentiation of pneumocytes[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	The MEK inhibitor CI-1040 is dissolved in DMSO as 10 mM stock solutions and used in cell culture at final concentration 50 mg/mL. U-937 cells are pretreated for 24 hrs with 5 and 20 uM CI- 1040, then transfected with wt-p53 siRNA or PUMA siRNA for 48 hrs. Then 20 mL of MTT solution are added to each well and incubated further for 2 hours. Upon termination, the supernatant is aspirated and the MTT formazan formed by metabolically viable cells is dissolved in 100 mL of isopropanol. The plates are mixed for 30 minutes on a gyratory shaker, and absorbance is measured at 595 nm using a plate reader[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice: The lung cancer mouse model is generated by targeting constitutively active C-Raf kinase to the lung. BAY 43-9006 or CI-1040 is daily intraperitoneal injected at a dose of 100 mg/kg from 4 months of age over a period of 21 days. Lungs were isolated and analyzed at the end of the treatment period[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Methods. 2023 Nov 2.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Clin Cancer Res. 2020 Apr 15;26(8):2011-2021.
- Int J Biol Macromol. 2020 May 1;150:261-280.
- Int J Biol Macromol. 2018 Dec;120(Pt A):1039-1047.

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REFERENCES

[1]. Allen LF, et al. CI-1040 (PD184352), a targeted signal transduction inhibitor of MEK (MAPKK). Semin Oncol. 2003 Oct;30(5 Suppl 16):105-16.

[2]. Wei CR, et al. MEK inhibitor CI-1040 induces apoptosis in acute myeloid leukemia cells in vitro. Eur Rev Med Pharmacol Sci. 2016 May;20(10):1961-8.

[3]. Kramer BW, et al. Use of mitogenic cascade blockers for treatment of C-Raf induced lung adenoma in vivo: CI-1040strongly reduces growth and improves lung structure. BMC Cancer. 2004 Jun 1;4:24.

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