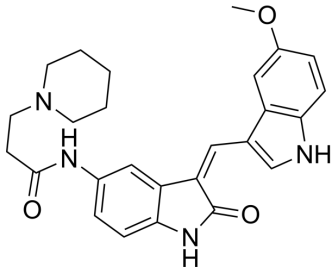
DEL-22379

Cat. No.:	HY-18932
CAS No.:	181223-80-3
Molecular Formula:	$C_{26}H_{28}N_4O_3$
Molecular Weight:	444.53
Target:	ERK; Apoptosis
Pathway:	MAPK/ERK Pathway; Stem Cell/Wnt; Apoptosis
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 (224.96 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2496 mL	11.2478 mL	22.4957 mL
5 mM	0.4499 mL	2.2496 mL	4.4991 mL
10 mM	0.2250 mL	1.1248 mL	2.2496 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 (5.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

DEL-22379 is an ERK dimerization Inhibitor. DEL-22379 readily binds to ERK2 with a K_d estimated in the low micromolar range, though binding is detectable even at low nanomolar concentrations. ERK2 dimerization is progressively inhibited with an IC_{50} of ~0.5 μM.

IC_{50} & Target

ERK2
0.5 μM (IC_{50})

In Vitro

DEL-22379 is an ERK dimerization inhibitor. DEL-22379 abolishes EGF-induced co-immunoprecipitation of ectopic ERK2 molecules tagged with hemagglutinin (HA) or FLAG epitopes, with an estimated half-maximal inhibitory concentration (IC_{50}) of ~0.5 μM. DEL-22379 inhibits growth of tumor cells harboring RAS-ERK pathway oncogenes. The biological effects of DEL-22379 are investigated on tumor cells in culture. The cytostatic effects of DEL-22379 are compared to those of the MEK inhibitor PD-0325901 and the ERK kinase inhibitor SCH-772984, as reflected by their half-maximal growth inhibitory

	concentrations (GI_{50}). Cell lines harboring mutant BRAF are the most sensitive to the three compounds. In comparison, wild-type (WT) cell lines for BRAF and RAS are the most resistant, and RAS mutant cells exhibit a range of sensitivities. In cells showing different oncogenic genotypes, distinct sensitivity to DEL-22379 can not be attributed to variations on its effects on dimerization, because DEL-22379 displays similar dimerization- and cytoplasmic signaling-inhibitory dose responses (IC_{50} of 150-400 nM) regardless of the genotype[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	To test DEL-22379 antitumor effects, some of the aforementioned cell lines are xenografted into nude mice, and tumor growth is monitored after intra-peritoneal administration of DEL-22379 at 15 mg/kg. At such a dose, inhibition of ERK dimerization is evident in liver extracts and in xenografted tumors. DEL-22379 markedly inhibits tumor progression for A375 cells (BRAF mutant)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	HEK293T cells are plated at a density of 1,000-2,000 cells/well and treated with DEL-22379 (0.2-1 μ M) for 48 hr, Alamar Blue is added, and the colorimetric change is measured at 570 and 600 nm. GI_{50} is estimated by nonlinear regression using GraphPad5 Prism Software. Apoptosis is analyzed by evaluating caspase 3 activity, either by western blotting or using the Caspase-Glo 3/7 luminogenic assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Cancer cells are xenografted in female, athymic nu/nu mice of 8 weeks of age. 3×10^6 cells are injected subcutaneously in the lateral flank and allowed to develop for 10-15 days before treatment with DEL-22379 at 15 mg/kg every 12 hr for 2 weeks. patient-derived xenografts (PDXs) are performed using patient-derived colorectal cancer cells harboring BRAFV600E from non-necrotic areas of primary adenocarcinomas from patients that undergo surgical resection. Cells are grafted in both flanks or in the cecum of NOD-SCID mice. DEL-22379 is administered by intra-peritoneal injection at a concentration of 15 mg/kg every 12 hr for 30 days[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biomed Pharmacother. 2023 Oct 18:168:115729.

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REFERENCES

[1]. Herrero A, et al. Small Molecule Inhibition of ERK Dimerization Prevents Tumorigenesis by RAS-ERK Pathway Oncogenes. Cancer Cell. 2015 Aug 10;28(2):170-82.

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