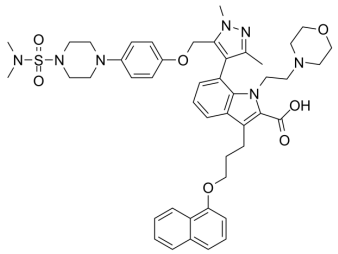
A-1210477

Cat. No.:	HY-12468
CAS No.:	1668553-26-1
Molecular Formula:	$C_{46}H_{55}N_7O_7S$
Molecular Weight:	850.04
Target:	Bcl-2 Family; Apoptosis
Pathway:	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 : 10 mg/mL (11.76 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1764 mL	5.8821 mL	11.7642 mL
	5 mM	0.2353 mL	1.1764 mL	2.3528 mL
	10 mM	0.1176 mL	0.5882 mL	1.1764 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: ≥ 1 mg/mL (1.18 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1 mg/mL (1.18 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (1.18 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

A-1210477 is a potent and selective inhibitor of MCL-1 with a K_i of 0.45 nM[1]. A-1210477 specifically binds MCL-1 and promotes apoptosis of cancer cells in an MCL-1-dependent manner[2].

IC_{50} & Target

Mcl-1	Bcl-2	Bfl-1	Bcl-W
0.45 nM (Ki)	132 nM (Ki)	660 nM (Ki)	2280 nM (Ki)

Apoptosis

In Vitro	A-1210477 (10 μM) reduces the amount of BIM co-immunoprecipitated with MCL-1 antibody, and triggers MCL-1 elevation in a variety of cancer cell lines, including the breast cancer cell line HCC-1806. A-1210477 inhibits MCL-1-NOXA interactions with an IC_{50} of approximately 1 μM, while having no effect on BCL-2-BIM or BCL-XL-BCL-XS interactions. The NSCLC cell lines H2110 and H23 are sensitive to A-1210477 with cell viability IC_{50}<10 μM, confirming that A-1210477 can kill MCL-1-dependent cell lines[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	TR-FRET-binding affinity assays are performed for BCL-2, BCL-XL, and MCL-1 in 4.52 mM monobasic potassium phosphate, 15.48 mM dibasic potassium phosphate, 1 mM sodium EDTA, 0.05% Pluronic F-68 detergent, 50 mM sodium chloride, and 1 mM DTT (pH 7.5) for BCL-XL.6 For MCL-1 assays, GST-tagged MCL-1 (1 nM) is mixed with 100 nM f-Bak, 1 nM Tb-labeled anti-GST antibody, and compound at room temperature (RT) for 60 min. Fluorescence is measured on an Envision plate reader using a 340/35 nm excitation filter and 520/525 (f-Bak) and 495/510 nm (Tb-labeled anti-GST antibody) emission filters. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Adherent cell lines are seeded at 50 000 cells per well in 96-well plates and treated for 48 h with compounds diluted in half-log steps starting at 30 μM and ending at 0.001 μM. Multiple myeloma cell lines are seeded at 15 000-20 000 cells per well and treated similarly. Effects on proliferation and viability are determined using CellTiter-Glo reagent from Promega according to the manufacturer's instructions. IC_{50} values are determined by non-linear regression analysis of the concentration response data. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Differ. 2019 Mar;26(3):470-486.
- Cell Death Dis. 2021 Aug 12;12(8):789.
- Cell Death Dis. 2020 Nov 15;11(11):982.
- Biochem Pharmacol. 2022 May;199:115017.
- Open Biol. 2016 Aug;6(8). pii: 160134.

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REFERENCES

[1]. Leverson JD, et al. Potent and selective small-molecule MCL-1 inhibitors demonstrate on-target cancer cell killing activity as single agents and in combination with ABT-263 (navitoclax). Cell Death Dis. 2015 Jan 15;6:e1590.

[2]. Qing Wang, et al. A-1210477, a selective MCL-1 inhibitor, overcomes ABT-737 resistance in AML. Oncol Lett. 2019 Nov;18(5):5481-5489.

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