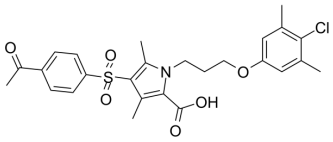
Mcl-1 inhibitor 6

Cat. No.:	HY-132307
CAS No.:	2598978-56-2
Molecular Formula:	$C_{26}H_{28}ClNO_6S$
Molecular Weight:	518.02
Target:	Bcl-2 Family; Apoptosis
Pathway:	Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (193.04 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9304 mL	9.6521 mL	19.3043 mL
	5 mM	0.3861 mL	1.9304 mL	3.8609 mL
	10 mM	0.1930 mL	0.9652 mL	1.9304 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Mcl-1 inhibitor 6 is an orally active, selective myeloid cell leukemia 1 (Mcl-1) protein inhibitor with a K_d of 0.23 nM and a K_i of 0.02 μM. Mcl-1 inhibitor 6 possesses superior selectivity over other Bcl-2 family members (Bcl-2, Bcl2A1, Bcl-xL, and Bcl-w, K_d >10 μM). Mcl-1 inhibitor 6 is a potent antitumor agent[1].

IC_{50} & Target

Mcl-1 0.23 nM (Kd)	Mcl-1 0.02 μM (Ki)	Bcl-2 >10 μM (Kd)	Bcl-2 10 μM (Ki)
Bcl2A1 >10 μM (Kd)	Bcl-xL >10 μM (Kd)	Bcl-W >10 μM (Kd)	Bfl-1 1.57 μM (Ki)

In Vitro

Mcl-1 inhibitor 6 has K_is of 10 μM and 1.57μM for Bcl-2 and Bfl-1, respectively[1].

Mcl-1 inhibitor 6 (1, 5 μM; for 48 h) significantly induces apoptosis in a concentration-dependent manner[1].

Mcl-1 inhibitor 6 (0.1, 5 μM; for 4 h) remarkably upregulates PARP cleavage in H929 cells in a concentration-dependent manner[1].

Mcl-1 inhibitor 6 (for 72 h) shows antiproliferative activities against the tumor cell lines (H929, MV4-11, SK-BR-3, NCI-H23; IC

$_{50}$=0.36-3.02 μM). Mcl-1 inhibitor 6 shows ideal selectivity against CML cell line K562 (IC_{50}>30 μM)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	H929 cells
Concentration:	1, 5 μM
Incubation Time:	For 48 hours
Result:	Significantly induced apoptosis in a concentration-dependent manner.

Western Blot Analysis[1]

Cell Line:	H929 cells
Concentration:	0.1, 0.5, 1, 5 μM
Incubation Time:	For 4 hours
Result:	Remarkably upregulated PARP cleavage in H929 cells in a concentration-dependent manner.

In Vivo

Mcl-1 inhibitor 6 (compound 40; 60 mg/kg with PO or 20 mg/kg with IP; every two days for 14 days) shows desired in vivo tumor growth inhibition activity[1].
Mcl-1 inhibitor 6 (3 mg/kg with IV or 10 mg/kg with PO) has a $T_{1/2}$ of 2.3 hours, a CL of 15.18 mL/min•kg by IV[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Balb/c nude female mice (7 weeks) loaded with MV4-11 xenografts[1]
Dosage:	60 mg/kg (PO) or 20 mg/kg (IP)
Administration:	IP or PO; every two days for 14 days
Result:	Showed desired in vivo tumor growth inhibition activity (T/C = 37.30% and 5.52% by po and ip administration, respectively).

Animal Model:	SD rats (200-250 g)[1]
Dosage:	3 mg/kg (IV) or 10 mg/kg (PO) (Pharmacokinetic Analysis)
Administration:	IV or PO
Result:	Had a $T_{1/2}$ of 2.3 hours, a CL of 15.18 mL/min•kg by IV. Had a $T_{1/2}$ of 2.1 hours, a CL of 36.8 mL/min•kg and a C_{max} of 2012.95 ng/mL.

REFERENCES

[1]. Peng-Ju Zhu, et al. Discovery of 3,5-Dimethyl-4-Sulfonyl-1 H-Pyrrole-Based Myeloid Cell Leukemia 1 Inhibitors with High Affinity, Selectivity, and Oral Bioavailability. J Med Chem. 2021 Aug 12;64(15):11330-11353.

Caution: Product has not been fully validated for medical applications. For research use only.

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