AZD5582

Cat. No.: HY-12600

CAS No.: 1258392-53-8

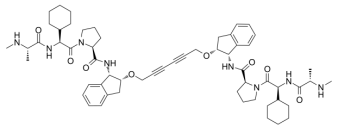
Molecular Formula: $C_{58}H_{78}N_8O_8$

Molecular Weight: 1015.29

Target: IAP; Apoptosis

Pathway: Apoptosis

Storage: 4°C, protect from light, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (98.49 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	0.9849 mL	4.9247 mL	9.8494 mL
	5 mM	0.1970 mL	0.9849 mL	1.9699 mL
	10 mM	0.0985 mL	0.4925 mL	0.9849 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 (2.46 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (2.46 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (2.46 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AZD5582 is an antagonist of the inhibitor of apoptosis proteins (IAPs), which binds to the BIR3 domains cIAP1, cIAP2, and XIAP with IC_{50}s of 15, 21, and 15 nM, respectively. AZD5582 induces apoptosis[1].

IC_{50} & Target

cIAP1	cIAP2	XIAP
15 nM (IC_{50})	21 nM (IC_{50})	15 nM (IC_{50})

In Vitro

AZD5582 (20 nM; 48 hours) inhibits cell viability by cooperation with IFNγ or viral double-stranded RNA (dsRNA) in H1975 NSCLC cells[2].

AZD5582 (20 nM; 17 or 25 hours) downregulates cIAP-1, activates RIPK1 (upstream regulator of caspase-8), and triggers the activation of extrinsic (caspase-8) and intrinsic (caspase-9) apoptosis pathways, causing the cleavage of caspase-3 and caspase-7[2].

AZD5582 (20 nM; 48 hours) involves in apoptosis due to induction of cell death and active caspase-3/8 activities by AZD5582 and IFNγ co-treatment in HCC827 NSCLC cells[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	H1975 NSCLC cell line
Concentration:	20 nM
Incubation Time:	48 hours
Result:	Cooperated with IFNγ or viral double-stranded RNA (dsRNA) to inhibit cell viability even cell death.

Apoptosis Analysis[2]

Cell Line:	HCC827 NSCLC cell line
Concentration:	20 nM
Incubation Time:	48 hours
Result:	Had an inhibitory effect on cell viability by cooperating with IFNγ.

Western Blot Analysis[2]

Cell Line:	H1975 NSCLC cell line
Concentration:	20 nM
Incubation Time:	17 or 25 hours
Result:	Down-regulated cIAP-1, activated RIPK1 (upstream regulator of caspase-8), triggered the cleavage (activation) of caspase-3,7,8 and 9.

In Vivo

AZD5582 (intravenous injection; 0.1-3.0 mg/kg; once a week; 2 weeks) causes degradation of cIAP1 and caspase 3 cleavage in tumor cells, and after a two-week treatment, the tumors largely resolved; when the mice are given a medium dose (0.5 mg/kg) of AZD5582, cIAP1 degrades after administration, but it takes a while time to reach apoptosis-inducing effect[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MDA-MB-231 xenograft-bearing mice[1]
Dosage:	0.1 mg/kg, 0.5 mg/kg, 3.0 mg/kg
Administration:	Intravenous injection; once a week; 2 weeks
Result:	Resulted in cIAP1 degradation and caspase-3 cleavage within tumor cells and causes substantial tumor regressions following two weekly doses of 3.0 mg/kg

CUSTOMER VALIDATION

- Cancer Immunol Res. 2023 Feb 8;CIR-22-0494.
- Mater Sci Eng C Mater Biol Appl. 29 December 2021, 112615.
- Biochim Biophys Acta Mol Basis Dis. 2019 Jun 26;1865(10):2618-2632.
- Cell Signal. 2020 Aug;72:109654.
- J Mol Med (Berl). 2022 Mar 5.

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REFERENCES

[1]. Hennessy EJ, et al. Discovery of a novel class of dimeric Smac mimetics as potent IAP antagonists resulting in a clinical candidate for the treatment of cancer (AZD5582). J Med Chem. 2013 Dec 27;56(24):9897-919.

[2]. Qin Hao, et al. IF-γ and Smac mimetics synergize to induce apoptosis of lung cancer cells in a TNFα-independent manner,Cancer Cell Int. 2018; 18: 84.

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