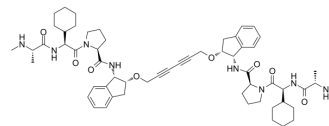


AZD5582

Cat. No.:	HY-12600
CAS No.:	1258392-53-8
Molecular Formula:	C ₅₈ H ₇₆ N ₈ O 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	Solvent \ Mass \ 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	<ol style="list-style-type: none"> 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 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 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] .		
IC₅₀ & Target	cIAP1 15 nM (IC ₅₀)	cIAP2 21 nM (IC ₅₀)	XIAP 15 nM (IC ₅₀)
In Vitro	AZD5582 (20 nM; 48 hours) inhibits cell viability by cooperation with IFN γ 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 IFN γ 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 IFN γ 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 IFN γ .

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

- 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 TNF α -independent manner, Cancer Cell Int. 2018; 18: 84.

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

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