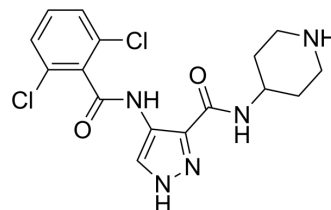


AT7519

Cat. No.:	HY-50940		
CAS No.:	844442-38-2		
Molecular Formula:	C ₁₆ H ₁₇ Cl ₂ N ₅ O ₂		
Molecular Weight:	382.24		
Target:	CDK; Apoptosis		
Pathway:	Cell Cycle/DNA Damage; Apoptosis		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	1 year
		-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (130.81 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.6161 mL	13.0806 mL	26.1613 mL
	5 mM	0.5232 mL	2.6161 mL	5.2323 mL
	10 mM	0.2616 mL	1.3081 mL	2.6161 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (6.54 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
 Solubility: ≥ 2.5 mg/mL (6.54 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (6.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AT7519 (AT7519M) as a potent inhibitor of CDKs, with IC₅₀s of 210, 47, 100, 13, 170, and <10 nM for CDK1, CDK2, CDK4 to CDK6, and CDK9, respectively.

IC₅₀ & Target

CDK9/Cyclin T 10 nM (IC ₅₀)	CDK5/p35 13 nM (IC ₅₀)	cdk2/cyclin A 47 nM (IC ₅₀)	Cdk4/cyclin D1 100 nM (IC ₅₀)
cdk6/cyclin D3	Cdk1/cyclin B	CDK7/Cyclin H/MAT1	GSK3β

	170 nM (IC ₅₀)	210 nM (IC ₅₀)	2400 nM (IC ₅₀)	89 nM (IC ₅₀)
In Vitro	<p>AT7519 (0-4 μM) results in dose-dependent cytotoxicity with IC₅₀s ranging from 0.5 to 2 μM in MM cells, and this induced cytotoxicity is associated with GSK-3β activation independent of transcriptional inhibition. AT7519 overcomes proliferative advantage conferred by cytokines and the protective effect of BMSC. AT7519 (0.5 μM) induces apoptosis of MM cells in a time-dependent manner. Moreover, AT7519 (0.5 μM) inhibits phosphorylation of RNA polymerase II CTD and partially inhibits RNA synthesis in MM.1S cells^[1]. AT7519 (250 nM) inhibits cell cycle progression in human tumor cell lines. AT7519 also induces apoptosis of human tumor cell lines^[2]. AT7519 (100-700 nM) induces apoptosis in leukemia cell lines. AT7519 also inhibits transcription in human tumor cell lines. Furthermore, AT7519 inhibits RNA polymerase II and reduces antiapoptotic protein levels^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>			
In Vivo	<p>AT7519 inhibits tumor growth in a human MM xenograft mouse model^[1]. AT7519 (4.6 and 9.1 mg/kg/dose) inhibits the growth of early-stage HCT116 tumor xenografts. AT7519 (10 mg/kg, i.p.) also inhibits the target CDKs in HCT116 tumor-bearing BALB/c nude mice^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>			

PROTOCOL

Cell Assay ^[1]	<p>AT7519's effects on viability of MM cell lines, primary MM cells, and PBMNCs is assessed by measuring 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrasodium bromide (MTT) dye absorbance. DNA synthesis is measured by tritiated thymidine uptake (3H-TdR). MM cells (2-3 × 10⁴ cells/well) are incubated in 96-well culture plates with media and different concentrations of AT7519 and/or recombinant IL-6 (10 ng/mL) or IGF-1 (50 ng/mL) for 24 or 48 h at 37°C and 3H-TdR incorporation is measured.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Administration ^[1]	<p>To evaluate the in vivo anti-MM activity of AT7519, male SCID mice are inoculated subcutaneously with 5×10⁶ MM.1S cells in 100 μL serum-free RPMI 1640 medium. When tumors are measurable, mice are treated intraperitoneally (IP) with vehicle or AT7519 dissolved in saline 0.9%. The first group of 10 mice is treated with 15 mg/kg once a day for five days for 2 weeks, and the second group is treated with 15 mg/kg once a day three times a week for four consecutive weeks. The control group receives the carrier alone at the same schedule. Tumor size is measured every alternate day in 2 dimensions using calipers, and tumor volume is calculated with the formula: $V = 0.5 a \times b^2$ (a= long diameter of the tumor, b= short diameter of the tumor). Animals are sacrificed when the tumor reaches 2 cm³ or when the tumor is ulcerated. Survival and tumor growth are evaluated from the first day of treatment until death.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Adv Sci (Weinh). 2024 Jan 6:e2305260.
- Cell Chem Biol. 2018 Feb 15;25(2):135-142.e5.
- Oncogene. 2023 Oct 16.
- FASEB J. 2024 Apr 30;38(8):e23628.

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REFERENCES

[1]. Santo L, et al. AT7519, A novel small molecule multi-cyclin-dependent kinase inhibitor, induces apoptosis in multiple myeloma via GSK-3beta activation and RNA polymerase II inhibition. *Oncogene*. 2010 Apr 22;29(16):2325-36.

[2]. Squires MS, et al. Biological characterization of AT7519, a small-molecule inhibitor of cyclin-dependent kinases, in human tumor cell lines. Biological characterization of AT7519, a small-molecule inhibitor of cyclin-dependent kinases, in human tumor cell lines.

[3]. Squires MS, et al. AT7519, a cyclin-dependent kinase inhibitor, exerts its effects by transcriptional inhibition in leukemia cell lines and patient samples. *Mol Cancer Ther*. 2010 Apr;9(4):920-8.

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

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite F, Monmouth Junction, NJ 08852, USA