



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

产品名称: **AT7519 (trifluoroacetate)**
产品别名: **AT7519 trifluoroacetate**

生物活性:				
Description	AT7519 trifluoroacetate as a potent inhibitor of CDKs, with IC ₅₀ s of 210, 47, 100, 13, 170, and <10 nM for CDK1, CDK2, CDK4 to CDK6, and CDK9, respectively.			
IC ₅₀ & Target	CDK9/Cyclin T	CDK5/p35	cdk2/cyclin A	Cdk4/cyclin D1
	10 nM (IC ₅₀)	13 nM (IC ₅₀)	47 nM (IC ₅₀)	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	AT7519 (0-4 μM) results in dose-dependent cytotoxicity with IC ₅₀ s 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] .			
In Vivo	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] .			
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.			
实验参考:				
Cell Assay	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 × 10 ⁴ 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. [1]			
	To evaluate the in vivo anti-MM activity of AT7519, male SCID mice are inoculated subcutaneously with 5×10 ⁶ 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			



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

Animal Administration	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. [1]
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.

源叶生物