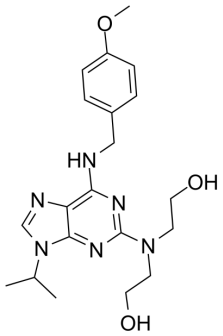
CVT-313

Cat. No.:	HY-15339
CAS No.:	199986-75-9
Molecular Formula:	$C_{20}H_{28}N_6O_3$
Molecular Weight:	400.47
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (249.71 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4971 mL	12.4853 mL	24.9707 mL
5 mM	0.4994 mL	2.4971 mL	4.9941 mL
10 mM	0.2497 mL	1.2485 mL	2.4971 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 (6.24 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.24 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CVT-313 (Cdk2 Inhibitor III) is a potent, selective, reversible, and ATP-competitive inhibitor of CDK2 with IC_{50} of 0.5 μM. CVT-313 inhibits CDC5L phosphorylation[1].

IC_{50} & Target			
	cdk2/cyclin A 0.5 μM (IC_{50})	Cdk1/cyclin B 4.2 μM (IC_{50})	Cdk4/cyclin D1 215 μM (IC_{50})

In Vitro	CVT-313 (Cdk2 Inhibitor III) has been shown to inhibit other kinases, but at much higher IC_{50} values, i.e., CDK1 (IC_{50}=4.2 μM), CDK4 D1 (IC_{50}=215 μM), and MAPK/PKA/PKC (IC_{50}>1.25 mM), compared to CDK2 (IC_{50}=0.5 μM). CVT-313 has been shown to have profound effects on cell proliferation at concentrations of 5-20 μM[1]. CVT-313 is a potent CDK2 inhibitor, which is identified from a purine analog library with an IC_{50} of 0.5 μM in vitro. Inhibition is competitive with respect to ATP (K_i=95 nM), and selective CVT-313 has no effect on other, nonrelated ATP-dependent serine/threonine kinases. When added to CDK1 or CDK4, a 8.5- and 430-fold higher concentration of CVT-313 is required for half-maximal inhibition of the enzyme activity. Using normal and tumor human/murine cell lines, the effects of CVT-313 on cell proliferation is measured. The IC_{50} for growth inhibition ranged from 1.25 to 20 μM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	For kinase assays, purified CDC5L(295-795)-His6 is mixed with [γ-^{32}P]ATP, COS-7 cell extract, and incubated in 100 μL 20 mM HEPES, pH 7.5, 50 mM NaCl, 2 mM $MnCl_2$, 10 mM $MgCl_2$, 0.5% NP-40, 0.5 mM PMSF, 5 mM benzamidine hydrochloride, 5 mM NaF, 1 mM $NaVO_3$ and the specific inhibitor at 30°C for 10 minutes. Cell extract as a source of kinase activity is prepared from subconfluent, serum-stimulated COS-7 cells lysed in 20 mM HEPES-NaOH, pH 7.5, 50 mM NaCl, 1% Triton X-100, 10% glycerol, protease and phosphotase inhibitors. Phosphorylated proteins are separated by electrophoresis in 15% polyacrylamide-SDS gels. Specific inhibitors included 20 μM staurosporine, 10 μM genistein, 1 μM CVT-313, 10 μM Rp-MB-cAMPS and 50 μM PD98059[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	MRC-5 cells are grown in Dulbecco's modified Eagle's medium containing 5% fetal calf serum. CVT313 (0, 5, 10, 15 μM) is added to exponentially growing cells in tissue culture. Cell population is measured. Proliferation assays are carried out using the nonradioactive CellTiter 96 kit after 48-h exposure. For FACS analysis of DNA content, cells are trypsinized, fixed in 70% ice-cold ethanol, and treated with 0.1 mg/mL RNase A and 40 μg/mL propidium iodide for 1 h at 37°C[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Arab J Chem. 2023 May 16, 104994.
- Int J Mol Sci. 2022 Feb 24;23(5):2493.
- Toxicol Appl Pharmacol. 2021 Oct 4;431:115739.
- Biomed Res Int. 2019 May 16;2019:2821731.

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REFERENCES

[1]. Graub R, et al. Cell cycle-dependent phosphorylation of human CDC5 regulates RNA processing. Cell Cycle. 2008 Jun 15;7(12):1795-803.

[2]. Brooks EE, et al. CVT-313, a specific and potent inhibitor of CDK2 that prevents neointimal proliferation. J Biol Chem. 1997 Nov 14;272(46):29207-11.

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