Olomoucine

Cat. No.: HY-W011428

CAS No.: 101622-51-9

Molecular Formula: $C_{15}H_{18}N_6O$

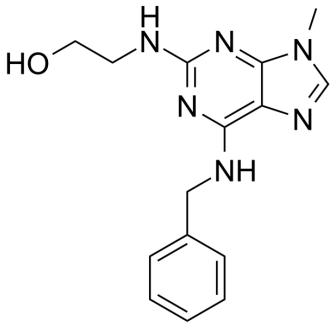
Molecular Weight: 298.34

Target: CDK

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 66.67 mg/mL (223.47 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.3519 mL	16.7594 mL	33.5188 mL
5 mM	0.6704 mL	3.3519 mL	6.7038 mL
10 mM	0.3352 mL	1.6759 mL	3.3519 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 (8.38 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (8.38 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Olomoucine is an ATP competitive inhibitor of CDKs. Olomoucine is a purine (HY-34431) derivative and inhibits CDC2/cyclin B, Cdk2/cyclin A, Cdk2/cyclin E (both IC_{50}=7 μM), CDK/p35 kinase (IC_{50}=3 μM) and ERK1/p44 MAP kinase (IC_{50}=25 μM)[1][2]. Olomoucine regulates cell cycle and shows anti-melanin tumor activity[3][4].

IC_{50} & Target

cdk2-cyclin A 7 μM (IC_{50})	cdk2-cyclin E 7 μM (IC_{50})	cdk5-p35 25 μM (IC_{50})

In Vitro

Olomoucine inhibits CDK2 and CDC2 kinases with IC_{50} of 7 μM (CDC2/cyclin B), 7 μM (CDK2/cyclin A), 7 μM (CDK2/cyclin E), 3 Mm (CDK5/p35), and 25μM (ERK1/p44 MAPK), respectively[1].
Olomoucine (0, 5, 10, 15, and 25 μM) is a competitive inhibitor for ATP and as a non-competitive inhibitor for histone H[1].
Olomoucine (0-1000 μM) inhibits DNA synthesis in interleukin-2-stimulated T lymphocytes (CTLL-2 cells) and triggers a Gl arrest similar to interleukin-2 deprivation[2].
Olomoucine (0-100 μM) inhibits Gl/S transition of non-small cell lung cancer cell line MB65 cells[2].
Olomoucine (0-150 μM) inhibits prophase/metaphase transition of Rdditapes oocytes[2].
Olomoucine inhibits tumor cells survival with IC_{50}s of 32.35 μM (dog melanoma), 42.15 μM (mouse B16 melanoma), 82.30 μM (human melanoma), respectively[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Olomoucine (8 mg/kg; i.v.; once daily; 7 d) induces apoptosis in tumor cells on the 3rd day after treatment without side effects[3].
Cassette dosing was found to overestimate the AUC while underestimating the Cmax compared with single dosing administration[4].

Cassette dosing pharmacokinetics for olomoucine[4]

Administration	C_{max} (nM)	Cl_{obs} (l/h)	V_{ss}(obs) (l)	MRT_{last} (h)	AUC_{inf}(obs) (nM·h)	$t_{1/2}$ (h)
cassettle	9208 (0.9)	1.10	0.67 (2.8)/td>	0.56	3030	1.03 (0.7)
single	7194 (0.6)	1.18	0.52 (2.1)/td>	0.40	2831	0.98 (0.7)

Note: Single agents dosing=50 mg/kg, cassette dosing=16.66 mg/kg.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Dog with spontaneous melanoma (oral and maxillofacial tumors)[3]
Dosage:	8 mg/kg
Administration:	Intravenous injection; once daily; for 7 days
Result:	Induced programmed cell death of cancer cells and resulted in rapid eradication of at least 68% of the tumor cells.

Animal Model:	Female Balb C− mice (6 weeks of age; weight of 20 g (±1.2 g))[4]
Dosage:	50 mg/kg (single agent) or 16.6 mg/kg combinded with purines (cassette)
Administration:	Intravenous injection (tail vein); samples taken at 0.25, 0.5, 1, 2, 4, 6, and 24 h post-dosing
Result:	Resulted faster plasma concentration decreasing with 50 mg/kg (as single agent) than 16.6 mg/kg (as cassette).

REFERENCES

[1]. Hajdúch M, et al. Induction of apoptosis and regression of spontaneous dog melanoma following in vivo application of synthetic cyclin-dependent kinase inhibitor olomoucine. Anticancer Drugs. 1997 Nov. 8(10):1007-13.

[2]. Raynaud FI, et al. Cassette dosing pharmacokinetics of a library of 2,6,9-trisubstituted purine cyclin-dependent kinase 2 inhibitors prepared by parallel synthesis. Mol

Cancer Ther. 2004 Mar. 3(3):353-62.

[3]. Vesely, J., Havlicek, J., Strnad, M., et al. Inhibition of cyclin-dependent kinases by purine analogues. European Journal of Biochemistry 224, 771-786 (1994).

[4]. Abraham, R.T., Acquarone, M., Andersen, A., et al. Cellular effects of olomoucine, an inhibitor of cyclin-dependent kinases. Biology of the Cell 83(2), 105-120 (1995).

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