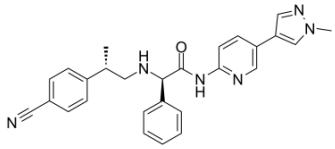
CPI-1612

Cat. No.:	HY-136285
CAS No.:	2374971-81-8
Molecular Formula:	$C_{27}H_{26}N_6O$
Molecular Weight:	450.53
Target:	Histone Acetyltransferase
Pathway:	Epigenetics
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 : 100 mg/mL (221.96 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2196 mL	11.0980 mL	22.1961 mL
	5 mM	0.4439 mL	2.2196 mL	4.4392 mL
	10 mM	0.2220 mL	1.1098 mL	2.2196 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: 5 mg/mL (11.10 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (11.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CPI-1612 is a highly potent, orally active EP300/CBP histone acetyltransferase (HAT) inhibitor with an IC_{50} of 8.1 nM for EP300 HAT. CPI-1612 has an anticancer activity[1].

IC_{50} & Target

IC50: 8.1 nM (EP300 HAT)[1]

In Vitro

CPI-1612 inhibits full length EP300 and full length CBP with IC_{50} values <0.5 nM and 2.9 nM, respectively[1].
CPI-1612 inhibits H3K18Ac MSD (H3K18 = histone 3 lysine 18, MSD = meso scale discovery) and JEKO-1 cell proliferation with with IC_{50} values 14 nM and <7.9 nM, respectively[1].
CPI-1612 (compound 17) shows weak activity in a hERG binding assay (IC_{50} = 10.4 μM) and displayed moderate inhibition of CYP2C8 (IC_{50} = 1.9 μM) and CYP2C19 (IC_{50} = 2.7 μM)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

CPI-1612 (compound 17; 0.5 mg/kg; oral administration; twice a day; for 4 weeks) treatment shows 67% tumor growth inhibition (TGI) with concomitant reduction of H3K27Ac in plasma and reduction of H3K18Ac in the tumor[1].

While the oral exposure of CPI-1612 (compound 17) in dogs (0.5 mg/kg IV; 1.0 mg/kg PO; clearance = 0.42 L/h/kg, V_{ss} = 3.7 L/kg, $T_{1/2}$ = 5.5 h, F% = 71; AUC/dose = 1691 h·mg/mL) and mice (1 mg/kg IV; 5 mg/kg PO; clearance = 3.8 L/h/kg, V_{ss} = 2.0 L/kg, $T_{1/2}$ = 0.98 h, F% = 79; AUC/dose = 211 h·mg/mL) is good, the exposure in rats is limited by poor bioavailability (1.0 mg/kg IV; 5.0 mg/kg PO; clearance = 2.6 L/h/kg, V_{ss} = 1.8 L/kg, $T_{1/2}$ = 1.2 h, F% = 9; AUC/dose = 35.6 h·mg/mL)[1].

A single dose of CPI-1612 is administered orally to CD-1 mice and brain and plasma exposures of CPI-1612 are measured at 0.25, 0.5, 1.0, 2.0, 4.0, and 8.0 h. CPI-1612 is highly brain-penetrant, showing a brain-to-plasma ratio of 0.35 after a single oral dose[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57B6 mice injected with JEKO-1 cells[1]
Dosage:	0.5 mg/kg
Administration:	Oral administration; twice a day; for 4 weeks
Result:	Showed 67% tumor growth inhibition (TGI) at a dose of 0.5 mg/kg.

REFERENCES

[1]. Jonathan E Wilson, et al. Discovery of CPI-1612: A Potent, Selective, and Orally Bioavailable EP300/CBP Histone Acetyltransferase Inhibitor. ACS Med Chem Lett. 2020 Apr 23;11(6):1324-1329.

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