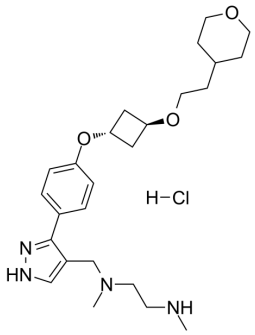
EPZ020411 hydrochloride

Cat. No.:	HY-12970A
CAS No.:	2070015-25-5
Molecular Formula:	$C_{25}H_{39}ClN_4O_3$
Molecular Weight:	479.06
Target:	Histone Methyltransferase; Apoptosis
Pathway:	Epigenetics; Apoptosis
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 1 years; -20°C, 6 months (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (104.37 mM; Need ultrasonic)

0.1 M HCL : 50 mg/mL (104.37 mM; ultrasonic and warming and adjust pH to 2 with HCl and heat to 60°C)

H_2O : 20 mg/mL (41.75 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0874 mL	10.4371 mL	20.8742 mL
	5 mM	0.4175 mL	2.0874 mL	4.1748 mL
	10 mM	0.2087 mL	1.0437 mL	2.0874 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 25 mg/mL (52.19 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.22 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.22 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.22 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

EPZ020411 hydrochloride is a selective inhibitor of PRMT6 with an IC_{50} of 10 nM, it has >10 folds selectivity for PRMT6 over PRMT1 and PRMT8. EPZ020411 hydrochloride can be used for the research of cancer[1][2].

IC_{50} & Target			
	PRMT6	PRMT1	PRMT8
	0.01 μM (IC_{50})	0.119 μM (IC_{50})	0.223 μM (IC_{50})

In Vitro

EPZ020411 hydrochloride (0-20 μM; 24 h) decreases H3R2 methylation in A375 cells[1].
EPZ020411 hydrochloride (20-40 μM; 6 h) reduces neomycin- and cisplatin-induced cell apoptosis and increases hair cell survival[2].

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

Western Blot Analysis[1]

Cell Line:	A375 cells
Concentration:	0-20 μM
Incubation Time:	24 hours
Result:	Dose-dependently decreased H3R2 methylation in A375 cells with an IC_{50} of 0.634 μM.

Cell Viability Assay[2]

Cell Line:	Cultured cochleae cells
Concentration:	20 and 40 μM
Incubation Time:	6 hours
Result:	Suppressed the apoptotic cascade induced by aminoglycosides and also inhibited cisplatin-induced apoptosis in the hair cells of the cochlear explants after pretreatment deposed. Reduced hair cell loss caused by cisplatin treatment.

In Vivo

EPZ020411 hydrochloride (10 mg/kg; i.p. once) reduces neomycin- and cisplatin-induced hearing loss in C57BL/6J wild-type mice with acute ototoxicity model[2].
Pharmacokinetic Parameters of EPZ020411 hydrochloride in rats[1].

	Rats IV 1 mg/kg	Rats SC 5 mg/kg
CL (mL/min/kg)	19.7±1.0	
V_{ss} (L/kg)	11.1±1.6	
$t_{1/2}$ (h)	8.54±1.43	9.19±1.60
t_{max} (h)		0.444
C_{max} (ng/mL)		844±306
$AUC_{0-\tau}$ (h·ng/mL)	745±34	2456±135
AUC_{0-inf} (h·ng/mL)	846±45	2775±181
F (%)		65.6±4.3

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

Animal Model:	C57BL/6J wild-type mice at P28 with acute ototoxicity model[2]

Dosage:	10 mg/kg
Administration:	Intraperitoneal injection; 10 mg/kg once
Result:	Significantly reduced neomycin- and cisplatin-induced HC loss and showed no effect without neomycin injection with mice.

CUSTOMER VALIDATION

- Acta Pharmacol Sin. 2021 Apr 13.
- EMBO Rep. 2018 Dec;19(12):e46377.
- Exp Cell Res. 2022 Nov 16;422(1):113413.

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REFERENCES

[1]. He Y, et al. Inhibition of Protein arginine methyltransferase 6 reduces reactive oxygen species production and attenuates aminoglycoside- and cisplatin-induced hair cell death. Theranostics. 2020 Jan 1;10(1):133-150.

[2]. Mitchell LH, et al. Aryl Pyrazoles as Potent Inhibitors of Arginine Methyltransferases: Identification of the First PRMT6 ToolCompound. ACS Med Chem Lett. 2015 Apr 6;6(6):655-659.

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