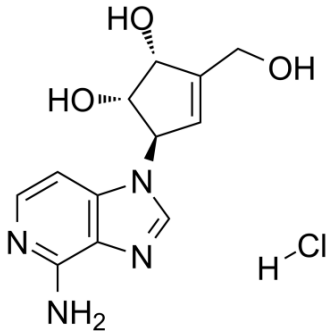
3-Deazaneplanocin A hydrochloride

Cat. No.:	HY-12186
CAS No.:	120964-45-6
Molecular Formula:	$C_{12}H_{15}ClN_4O_3$
Molecular Weight:	298.73
Target:	Histone Methyltransferase
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

H_2O : 50 mg/mL (167.38 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	3.3475 mL	16.7375 mL	33.4750 mL
5 mM	0.6695 mL	3.3475 mL	6.6950 mL
10 mM	0.3348 mL	1.6738 mL	3.3475 mL

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

BIOLOGICAL ACTIVITY

Description

3-Deazaneplanocin A hydrochloride (DZNep hydrochloride) is a potent histone methyltransferase EZH2 inhibitor[1][2]. 3-Deazaneplanocin A hydrochlorideis a potent S-adenosylhomocysteine hydrolase (AHCY) inhibitor[6].

In Vitro

3-Deazaneplanocin A (DZNep) hydrochloride is a potent histone methyltransferase EZH2 inhibitor. Treatment of OCI-AML3 cells with 3-Deazaneplanocin A (1.0 μM) results in a significant increase in accumulation of cells in the G_0/G_1 phase (58.5%) with a concomitant decrease in the number of cells in S phase (35.2%) and G_2/M phases (6.3%) of the cell cycle ($P<0.05$). Treatment with 3-Deazaneplanocin A (200 nM to 2.0 μM) for 48 hours, dose dependently, inhibits colony growth of OCI-AML3 and HL-60 cells[1]. 3-Deazaneplanocin A (DZNep) hydrochloride reduces the expression of EZH2, especially after 72 hours (e.g. 48%, 32% and 36% reduction of EZH2 in PANC-1, MIA-PaCa-2 and LPc006 cells, respectively)[2]. 3-Deazaneplanocin A (DZNep) hydrochloride shows minimal growth inhibition in PANC-1 cells. More than 50% of these cells are still growing after exposure at the highest concentration (20 μM). MIA-PaCa-2 and LPc006 cells are much more sensitive, with IC_0 values of 1.0±0.3 and 0.10±0.03 μM, respectively[2]. 3-Deazaneplanocin A (DZNep) hydrochloride causes dose-dependent inhibition of cell proliferation of NSCLC cell lines, and the IC_0 values range from 0.08 to 0.24 μM[3].

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

In Vivo	The survival of NOD/SCID mice with acute myeloid leukemia (AML) due to HL-60 cells is significantly higher, if treated with 3-Deazaneplanocin A (DZNep) and LBH589 (PS) compare to treatment with PS, 3-Deazaneplanocin A, or vehicle alone (P<0.05). Median survival is as follows: control, 36 days; PS, 42 days; 3-Deazaneplanocin A, 43 days; and 3-Deazaneplanocin A plus PS, 52 days[1]. There is a progressive increase in weight of rats treated with physiological saline in a time-dependent manner (the mean growth rate=3.19% per day). Administration of 20 mg/kg 3-Deazaneplanocin A (DZNep) not only markedly reduces the relative weight of the rats compare to the initial weight (−2.0%, −4.9% and −1.2%) in the first three days post-treatment, but also suppresses the weight growth rate to 2.6% per day from the fourth day onwards post-dose[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	AML HL-60 cells are obtained and maintained. OCI-AML-3 cells are cultured in α minimum essential medium with 10% fetal bovine serum, and 1% nonessential amino acids. To analyze synergism between 3-Deazaneplanocin A and PS in inducing apoptosis, cells are treated with 3-Deazaneplanocin A (100-750 nM) and PS (5-20 nM) at a constant ratio for 48 hours. The percentage of apoptotic cells is determined by flow cytometry. The combination index (CI) for each drug combination is obtained by median dose effect of Chou and Talalay, using the CI equation within the commercially available software Calcusyn[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][4]	Mice[1] HL-60 cells (5 million) are injected into the tail vein of female nonobese diabetic/severe combined immunodeficiency (NOD/SCID) mice, and the mice are monitored for 7 days. The following treatments are administered in cohorts of 7 mice for each treatment: vehicle alone, 1 mg/kg 3-Deazaneplanocin A, 10 mg/kg PS, and 3-Deazaneplanocin A plus PS. Treatments are initiated on day 7. 3-Deazaneplanocin A is administered twice per week (Tuesday-Thursday) intraperitoneally for 2 weeks, and then discontinued. PS is administered 3 days per week (Monday, Wednesday, and Friday) for 4 weeks. The survival of mice from the tail vein model is represented with a Kaplan-Meier survival plot. Rats[4] Male wistar rats are used. The acute toxicity study is carried out to determine the NOAEL of 3-Deazaneplanocin A in rats. In total, 20 rats are divided into 4 groups of five each. Three groups are intravenously administered 20, 15, 10 mg/kg body weight (BW) DZNep solution by the tail vein. The remaining group is given physiological saline (0.9% NaCl saline) as the control group. Then, the NOAEL of free DZNep is determined, depending on the following endpoint parameters obtained. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2021 Feb 23;12(1):1237.
- J Immunother Cancer. 2019 Nov 14;7(1):300.
- J Am Soc Nephrol. 2016 Jul;27(7):2021-34.
- Cell Death Dis. 2020 Oct 23;11(10):906.
- Apoptosis. 2020 Oct;25(9-10):697-714.

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[1]. Fiskus W, et al. Combined epigenetic therapy with the histone methyltransferase EZH2 inhibitor 3-deazaneplanocin A and the histone deacetylase inhibitor LBH589 against human AML cells. Blood, 2009, 114(13), 2733-2743.

[2]. Avan A, et al. Molecular mechanisms involved in the synergistic interaction of the EZH2 inhibitor 3-deazaneplanocin A with LY 188011 in pancreatic cancer cells. Mol Cancer Ther. 2012 Aug;11(8):1735-46.

[3]. Kikuchi J, et al. Epigenetic therapy with 3-deazaneplanocin A, an inhibitor of the histone methyltransferase EZH2, inhibits growth of non-small cell lung cancer cells. Lung Cancer. 2012 Nov;78(2):138-43.

[4]. Sun F, et al. Preclinical pharmacokinetic studies of 3-deazaneplanocin A, a potent epigenetic anticancer agent, and its human pharmacokinetic prediction using GastroPlus?. Eur J Pharm Sci. 2015 Sep 18;77:290-302.

[5]. Noriko Uchiyama, et al. Aristeromycin and DZNeP cause growth inhibition of prostate cancer via induction of mir-26a. Eur J Pharmacol. 2017 Oct 5;812:138-146.

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