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产品名称：2-Pyrimidone-1-Beta-D-Riboside
产品别名：泽布拉林 ；Zebularine；NSC309132; 4-Deoxyuridine

生物活性：

Description	Zebularine (NSC309132; 4-Deoxyuridine) is a DNA methyltransferase inhibitor. Zebularine also inhibits cytidine deaminase with a Ki of 0.95 μM.

IC_{50} & Target	DNMT1	DNMT3a/3L	Cytidine deaminase	Autophagy
			0.95 μM (Ki)	

In Vitro	Zebularine exerts its demethylation activity by stabilizing the binding of DNMTs to DNA, hindering the methylation and decreasing the dissociation, thereby trapping the enzyme and preventing turnover even at other sites. zebularine enhances tumor cell chemo- and radiosensitivity and has antimitogenic and angiostatic activities[1]. Zebularine inhibits DNA methylation and reactivates a gene previously silenced by methylation. Zebularine induces the myogenic phenotype in 10T1/2 cells, which is a phenomenon unique to DNA methylation inhibitors. Zebularine reactivates a silenced p16 gene and demethylated its promoter region in T24 bladder carcinoma cells[2]. Zebularine treatment inhibits cell growth in a dose and time dependent manner with an IC50 of ~100 μM and 150 μM in MDA-MB-231 and MCF-7 cells, respectively, on 96 h exposure. At high doses zebularine induced changes in apoptotic proteins in a cell line specific manner manifested by alteration in caspase-3, Bax, Bcl2 and PARP cleavage[3]. Zebularine is also a potent competitive inhibitor of the enzyme CR deaminase. The Ki for zebularine is 0.95μM[4].
In Vivo	Zebularine is only slightly cytotoxic to tumor-bearing mice. Compared with those in control mice, tumor volumes are statistically significantly reduced in mice treated with high-dose zebularine administered by intraperitoneal injection or by oral gavage[2]. Zebularine also enhances the survival time of mice with L1210 leukemia treated with 5-AZA-CdR. About 27% of the mice treated with this drug combination has a survival time longer than the mice treated with only 5-AZA-CdR[4].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (438.21 mM)

H_2O : 50 mg/mL (219.11 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	4.3821 mL	21.9106 mL	43.8212 mL
5 mM	0.8764 mL	4.3821 mL	8.7642 mL
10 mM	0.4382 mL	2.1911 mL	4.3821 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现

	用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (10.96 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (10.96 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (10.96 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (10.96 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (10.96 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (10.96 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Champion C, et al. Mechanistic insights on the inhibition of c5 DNA methyltransferases by zebularine. PLoS One. 2010 Aug 24;5(8):e12388. [2]. Cheng JC, et al. Inhibition of DNA methylation and reactivation of silenced genes by zebularine. J Natl Cancer Inst. 2003 Mar 5;95(5):399-409. [3]. Billam M, et al. Effects of a novel DNA methyltransferase inhibitor zebularine on human breast cancer cells. Breast Cancer Res Treat. 2010 Apr;120(3):581-92. [4]. Lemaire M, et al. Inhibition of cytidine deaminase by zebularine enhances the antineoplastic action of 5-aza-2'-deoxycytidine. Cancer Chemother Pharmacol. 2009 Feb;63(3):411-6.

实验参考：

Cell Assay	For methylation analysis, 10T1/2 cells and T24 cells are treated with the various concentrations of zebularine. For 10T1/2 cells, the medium is changed 24 hours after the initial drug treatment, whereas for T24 cells, the medium is changed 24 hours or 48 hours after the initial drug treatment. DNA and RNA are harvested from 10T1/2 cells 72 hours after initial drug treatment and from T24 cells 96 hours after initial drug treatment. The methylation status of the indicated DNA regions is measured in two separate and independent experiments, both of which are done in duplicate[2].
Animal Administration	EJ6 cells (5×10^5/injection) suspended in PBS are inoculated subcutaneously into the right and left flanks (along the midaxillary lines) of 4- to 6-week-old male BALB/c nu/nu mice. Mice (n=30) are randomLy divided into six groups (intraperitoneal control, oral control, intraperitoneal zebularine at 500 mg/kg, oral zebularine at 500 mg/kg, intraperitoneal zebularine at 1000 mg/kg, and oral zebularine at 1000 mg/kg). Each group consisted of five mice (at least six tumors per group; one or two mice per group are randomLy killed at earlier time points to establish a time course of

	expression). After 2–3 weeks and after macroscopic tumors (50–200 mm^3) had formed, zebularine or control treatments are initiated. Zebularine, at doses of 500 mg/kg or 1000 mg/kg, is administered daily by intraperitoneal injection or oral gavage in a solution of 0.45% saline over a period of 18 days[2].
References	[1]. Champion C, et al. Mechanistic insights on the inhibition of c5 DNA methyltransferases by zebularine. PLoS One. 2010 Aug 24;5(8):e12388. [2]. Cheng JC, et al. Inhibition of DNA methylation and reactivation of silenced genes by zebularine. J Natl Cancer Inst. 2003 Mar 5;95(5):399-409. [3]. Billam M, et al. Effects of a novel DNA methyltransferase inhibitor zebularine on human breast cancer cells. Breast Cancer Res Treat. 2010 Apr;120(3):581-92. [4]. Lemaire M, et al. Inhibition of cytidine deaminase by zebularine enhances the antineoplastic action of 5-aza-2'-deoxycytidine. Cancer Chemother Pharmacol. 2009 Feb;63(3):411-6.