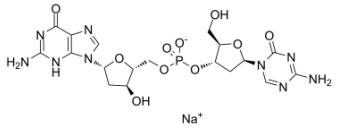
Guadecitabine sodium

Cat. No.:	HY-15229
CAS No.:	929904-85-8
Molecular Formula:	$C_{18}H_{23}N_9NaO_{10}P$
Molecular Weight:	579.39
Target:	DNA 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

DMSO : 50 mg/mL (86.30 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7260 mL	8.6298 mL	17.2595 mL
	5 mM	0.3452 mL	1.7260 mL	3.4519 mL
	10 mM	0.1726 mL	0.8630 mL	1.7260 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 (4.31 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

S-110 is a dinucleotide consisting of 5-Aza-CdR followed by a deoxyguanosine which shows to be an effective **DNA methylation inhibitor**.

IC_{50} & Target

DNMT1

In Vitro

After HCT116 colorectal carcinoma cells are treated for 6 days, a dose-dependent increase in p16expression is

	observed with S-110. In addition, T24 and HCT116 cells treated with S-110 or 5-aza-CdR for 3 days show a dose-dependent increase in the level of p16 protein, showing the competence of S-110 to inhibit DNA methylation and induce p16 at both mRNA and protein levels as well as 5-aza-CdR. Thus, S-110 is able to inhibit DNA methylation at 5′-region and induce the expression of the p16 gene in T24 and HCT116 cells at concentrations comparable to 5-aza-CdR, and the induction of p16 expression by both agents correlates with the demethylation at the 5′-end region of the gene in both cell lines. S-110 is slightly less toxic than 5-aza-CdR at the doses tested up to 1 μM concentration but displaying similar toxicity at 10 μM concentration[1].
In Vivo	S-110 at 10mg/kg is an effective dose at reducing DNA methylation and retarding tumor growth, and caused roughly the same level of toxicity as 5-Aza-CdR. S-110 is effective in vivo at reactivating the expression of the p16 gene, which is heavily methylated in the parent EJ6 cells. S-110 is effective in reducing the level of DNA methylation in vivo at the p16 promoter region. S-110 is better tolerated than 5-Aza-CdR in vivo, suggesting that it can be an attractive alternative for potential clinical use[2].

PROTOCOL

Cell Assay [1]	**T24 cells** are plated at a low density (100 per 60-mm dish) and treated with varying concentrations of 5-aza-CdR and **S-110 (0.1, 0.2, 10 μM**. Colonies are allowed to form for 10 to 14 days, fixed with methanol, and stained with 10% Giemsa. The number of colonies from an untreated control plate is used to calculate the plating efficiency in percent at each concentration. Triplicate dishes are used, and error bars are represented by 1 SD of the mean[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mouse: **Athymic nu/nu mice** are inoculated subcutaneously in the right hind flank with 10^7 EJ6 bladder cancer cells. After tumors reach 0.5 cm in diameter, animals are stratified into three groups with eight animals per group to begin treatments. Doses and dosing schedules are designed so that each group received molar equivalents of either S-110 or 5-Aza-CdR. The agents are administered **SQ once weekly at a dose of 12.2 mg/kg for S-110** and 5.0 mg/kg for 5-Aza-CdR for three weeks. The study includes an appropriate PBS control group. Tumor sizes by caliper and body weight measurements are taken twice weekly to monitor tumor growth inhibition and tolerability[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Yoo CB, et al. Delivery of 5-aza-2'-deoxycytidine to cells using oligodeoxynucleotides. Cancer Res. 2007 Jul 1;67(13):6400-8.

[2]. Chuang JC, et al. S-110, a 5-Aza-2'-deoxycytidine-containing dinucleotide, is an effective DNA methylation inhibitor in vivo and can reduce tumor growth. Mol Cancer Ther. 2010 May;9(5):1443-50.

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