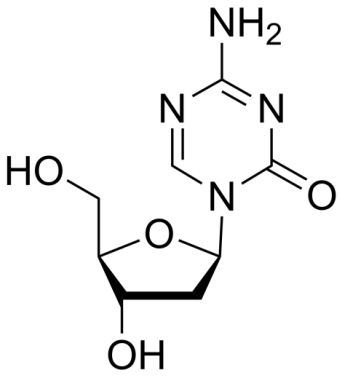
Data Sheet

Product Name:	Decitabine
Cat. No.:	CS-0372
CAS No.:	2353-33-5
Molecular Formula:	$C_8H_{12}N_4O_4$
Molecular Weight:	228.21
Target:	Apoptosis; DNA Methyltransferase; Nucleoside Antimetabolite/Analog
Pathway:	Apoptosis; Cell Cycle/DNA Damage; Epigenetics
Solubility:	DMSO : ≥ 50 mg/mL (219.10 mM); H2O : 20 mg/mL (87.64 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Decitabine (NSC 127716) is an orally active **deoxycytidine analogue antimetabolite** and a **DNA methyltransferase** inhibitor. Decitabine incorporates into DNA in place of cytosine can covalently trap **DNA methyltransferase** to DNA causing irreversible inhibition of the enzyme. Decitabine induces cell G2/M arrest and cell **apoptosis**. Decitabine has potent anticancer activity[1][2]. ***In Vitro:*** Decitabine treatment significantly inhibits cell growth of SNU719, NCC24 and KATOIII 96 hours after exposure to decitabine. Decitabine induces G2/M arrest and apoptosis in EBVaGC, inhibits invasion ability, and up-regulates E-cadherin expression for EBVaGC[1].

Only high concentrations (10 μM) Decitabine (0.1-1 μM; 24-72 hours) results in a G2 phase arrest, which is accompanied by a reduction of cells in G1 phase[3].

Decitabine up-regulates DCTPP1 and dUTPase expression in HeLa cells[4].

In Vivo: Decitabine (1.0 mg/kg, p.o.) in combination with tetrahydrouridine (THU) causes severe toxicity occurs in female CD-1 mice, and results in an increased sensitivity to decitabine toxicity correlating with decitabine plasma levels[5].

Decitabine (1.0 mg/kg; i.p.; once daily for 5 consecutive days) leads to regression of EL4 tumors established in C57BL/6 Mice[7].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [3]The pyrophosphohydrolase activity of DCTPP1 is determined using a continuous spectrophotometric assay. In a standard reaction (1 mL final volum), 10-250 μM of the nucleotide substrate is incubated in reaction buffer (20 mM $MgCl_2$, 100 mM KCl, 0.75 mg/mL BSA and 4 mM DTT) with concentrations ranging from 0.1-1 μM of DCTTP1. All reactions are carried out at 25°C. **Cell Assay:** Decitabine is dissolved in PBS.[1]Cell viability is analyzed by cell count and MTS assay. SNU719, NCC24 and KATOIII are seeded at a density of 5×10^4 cells/mL and cultured with only RPMI-1640 supplemented with FBS for 24 hours. After 24 hours of incubation, cells are treated in the presence or absence of Decitabine (DAC) for 120 hours. Cells for cell counts are trypsinized and counted at 0, 24, 48, 72, 96 and 120 hours after DAC treatment. Viable cells are determined by trypan blue exclusion. For MTS assay, cells (SNU719 and NCC24: $1x10^4$/well, KATOIII: $1x10^3$/well) are eeded onto 96-well dishes. After seeding, MTS is added into the well at the indicated period. After incubation for 1 hour, the absorbance is measured at 490 nm. **Animal Administration:** [4]Mice are assigned to four dose groups and a vehicle control group. Animals are gavaged with Decitabine (DAC) or its vehicle 1 hour ± 5 minutes after administration of tetrahydrouridine (THU) or its vehicle at a dose volume of 10 mL/kg. The DAC doses are selected based on the range finding study in which the mice tolerated six oral doses (2x/week) of 0.1, 0.2 and 0.4 mg/kg DAC in combination with a fixed dose of 167 mg/kg THU. A fixed THU dose (500 mg/m^2) and the optimal timing between THU and DAC administration (60 min) are selected. Conversion of milligrams per body surface area dose in mice into milligrams per kilogram body weight dose estimation is based on Michaelis constant (K_m) values for mice. In brief, the mouse dose in milligrams per body surface area (500

mg/m^2) is divided by the K_m of 3 to convert the dose to milligrams per kilogram body weight (167 mg/kg). The working body weight range of mice in the guideline is 11-34 gram; the body weight range of mice used in this study is 24-38 gram.

References:

[1]. Nakamura M, et al. Decitabine inhibits tumor cell proliferation and up-regulates E-cadherin expression in Epstein-Barr virus-associated gastric cancer. J Med Virol. 2016 Jul 19.

[2]. Hagemann S, et al. Azacytidine and decitabine induce gene-specific and non-random DNA demethylation in human cancer cell lines. PLoS One. 2011 Mar 7;6(3):e17388.

[3]. Requena CE, et al. The nucleotidohydrolases DCTPP1 and dUTPase are involved in the cellular response to decitabine. Biochem J. 2016 Jun 20.

[4]. Terse P, et al. Subchronic oral toxicity study of decitabine in combination with tetrahydrouridine in CD-1 mice. Int J Toxicol. 2014 Mar-Apr;33(2):75-85.

[5]. Yu J, et al. DNA methyltransferase expression in triple-negative breast cancer predicts sensitivity to decitabine. J Clin Invest. 2018 Jun 1;128(6):2376-2388.

[6]. Wang LX, et al. Low dose decitabine treatment induces CD80 expression in cancer cells and stimulates tumorspecific cytotoxic T lymphocyte responses. PLoS One. 2013 May 9;8(5):e62924.

[7]. Parker WB. Enzymology of purine and pyrimidine antimetabolites used in the treatment of cancer. Chem Rev. 2009 Jul;109(7):2880-93.

CAIndexNames:

1,3,5-Triazin-2(1H)-one, 4-amino-1-(2-deoxy-.beta.-D-erythro-pentofuranosyl)-

SMILES:

O[C@H]1C[C@H](N2C(N=C(N)N=C2)=O)O[C@@H]1CO

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