Product Data Sheet

Product Name: CNDAC
Cat. No.: GC33177

Chemical Properties

Cas. No.	135598-68-4		
SMILES	O=C(N=C(N)C=C1)N1[C@H]2[C@@H](C#N)[C@H](O)[C@@H](CO)O2		
Formula	$C_{10}H_{12}N_4O_4$	M.Wt	252.23
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	CNDAC		

Protocol

Cell experiment:

1×106 primary BM and PB cells are treated with 1 μM (low), 10 μM (medium), and 100 μM (high) of ara-C or CNDAC or 0.005 μM (low), 0.05 μM (medium) and 0.5 μM (high) mitoxantrone in 24 well plates at 37°C, 5% CO2, and 100% humidity for 4 days. Appropriate untreated controls are included. Postdrug treatment, both PB and BM non-adherent cells are washed to remove compound, replated on M2-10B4 stromal layers, and reincubated at 37°C, 5% CO2, 100% humidity. Cells are analyzed immediately posttreatment and following 3, 7, and 31 days postdrug removal.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

References:

[1]. Liu XJ, et al. Sapacitabine, the prodrug of CNDAC, is a nucleoside analog with a unique action mechanism of inducing DNA strand breaks. hin J Cancer. 2012 Aug;31(8):373-80.
[2]. Jagan S, et al. Bone Marrow and Peripheral Blood AML Cells Are Highly Sensitive to CNDAC, the Active Form of Sapacitabine. Adv Hematol. 2012;2012:727683.
[3]. Liu X, et al. Homologous recombination as a resistance mechanism to replication-induced double-strand breaks caused by the antileukemia agent CNDAC. Blood. 2010 Sep 9;116(10):1737-46.

Background

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CNDAC is a major metabolite of oral drug sapacitabine, and a nucleoside analog.

CNDAC-induced SSBs can be repaired by the transcription-coupled nucleotide excision repair pathway, whereas lethal DSBs are mainly repaired through homologous recombination. Deficiency in two Rad51 paralogs, Rad51D and XRCC3, greatly sensitize cells to CNDAC. The Rad51D-null cell line is approximately 50-fold more sensitive to CNDAC (IC50=0.006 μM) compared to 51D1.3, the Rad51D-repleted line (IC50=0.32 μM) [1]. CNDAC shows inhibitory activity against HL-60 and THP-1 cells with IC50s of 1.58 μM and 0.84 μM. CNDAC (10 μM) results in a significant drop in cell survival compared to the untreated on days 4, 7, and 14. CNDAC is more effective at reducing viability and inducing apoptosis than ara-C at equivalent concentrations in the THP-1 cell line, which is defined as displaying resistance to ara-C[2]. CNDAC induces DSBs, which are products of replication, rather than a consequence of induction of apoptosis. CNDAC causes DNA damage, and DNA-PK and ATR are dispensable for cell survival. CNDAC exhibits potent activity against human fibroblasts deficient in ATM or transfected with an empty vector, approximately 30-fold more than cells repleted with full-length ATM cDNA, with IC50s of 0.01 μM and 0.3 μM, respectively. CNDAC-induced DNA damage is repaired through the homologous recombination pathway[3].

[1]. Liu XJ, et al. Sapacitabine, the prodrug of CNDAC, is a nucleoside analog with a unique action mechanism of inducing DNA strand breaks. hin J Cancer. 2012 Aug;31(8):373-80. [2]. Jagan S, et al. Bone Marrow and Peripheral Blood AML Cells Are Highly Sensitive to CNDAC, the Active Form of Sapacitabine. Adv Hematol. 2012;2012:727683. [3]. Liu X, et al. Homologous recombination as a resistance mechanism to replication-induced double-strand breaks caused by the antileukemia agent CNDAC. Blood. 2010 Sep 9;116(10):1737-46.

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