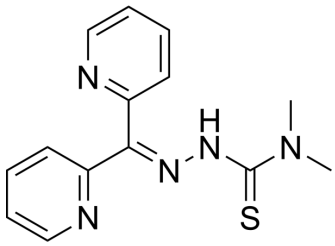
Dp44mT

Cat. No.:	HY-18973
CAS No.:	152095-12-0
Molecular Formula:	$C_{14}H_{15}N_5S$
Molecular Weight:	285.37
Target:	Apoptosis; Ferroptosis
Pathway:	Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (350.42 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.5042 mL	17.5211 mL	35.0422 mL
	5 mM	0.7008 mL	3.5042 mL	7.0084 mL
	10 mM	0.3504 mL	1.7521 mL	3.5042 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 (8.76 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.76 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Dp44mT is an iron chelator with selective anticancer activity.

IC_{50} & Target

Target: Iron chelator[1]

In Vitro

Dp44mT is cytotoxic to breast cancer cells, at least in part, due to selective inhibition of top2α. Dp44mT alone induced selective cell killing in the breast cancer cell line MDA-MB-231 when compared with healthy mammary epithelial cells (MCF-12A). It induces G1 cell cycle arrest and reduces cancer cell clonogenic growth at nanomolar concentrations. Dp44mT, but not the iron chelator desferal, induces DNA double-strand breaks quantified as S139 phosphorylated histone foci (γ-H2AX) and Comet tails induced in MDA-MB-231 cells. Doxorubicin-induced cytotoxicity and DNA damage are both enhanced significantly in the presence of low concentrations of Dp44mT. The chelator caused selective poisoning of DNA

topoisomerase IIα (top2α) as measured by an in vitro DNA cleavage assay and cellular topoisomerase-DNA complex formation[1]. Dp44mT targets lysosome integrity through copper binding. Copper binding is essential for the potent antitumor activity of Dp44mT, as coincubation with nontoxic copper chelators markedly attenuated its cytotoxicity[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

For DNA topoisomerase IIα assays, the 161-bp fragment from pBluescript SK(-) phagemid DNA or single stranded oligonucleotides are 5'-end labeled with [^{32}P]ATP and T4 polynucleotide kinase. Labeling mixtures are subsequently centrifuged through Mini Quick Spin DNA columns (for pSK fragments) or Oligo columns (for oligonucleotides) to remove the unincorporated label. Annealing to the complementary strand of the oligonucleotides is done by heating the reaction mixture to 95°C and overnight cooling to room temperature in 10 mM Tris-HCl (pH 7.8), 100 mM NaCl, and 1 mM EDTA. DNA substrates (10 pmol/reaction) are incubated with 500 ng of top2a or top2h in the presence or absence of Dp44mT for the indicated times at 25°C in 10 µL of reaction buffer. Reactions are stopped by adding SDS (final concentration 0.5%). Samples are separated on 16% (for pSK DNA) or 20% (for the oligonucleotides) denaturing polyacrylamide gels (7 M urea). Imaging and quantitation are done using a PhosphorImager[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [1]

Cell proliferation is measured using a sulforhodamine B dye–based assay. MDA-MB-231(breast cancer) and MCF-12A (healthy mammary epithelial) cells are incubated with increasing concentrations of Dp44mT (0.01, 0.1, 1, 10, 100 µM). Results are expressed relative to control[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Signal. 2023 Jul 3;110791.
- Università Vita-Salute San Raffaele. 2022 Apr 08. 34.
- bioRxiv. 2020 Jun.

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REFERENCES

[1]. Rao VA, et al. The iron chelator Dp44mT causes DNA damage and selective inhibition of topoisomerase IIalpha in breast cancer cells. Cancer Res. 2009 Feb 1;69(3):948-57.

[2]. Lovejoy DB, et al. Antitumor activity of metal-chelating compound Dp44mT is mediated by formation of a redox-active copper complex that accumulates in lysosomes. Cancer Res. 2011 Sep 1;71(17):5871-80.

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