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Daun02

Cat. No.: HY-13061

CAS No.: 290304-24-4

Molecular Formula: $C_{41}H_{44}N_2O_{20}$

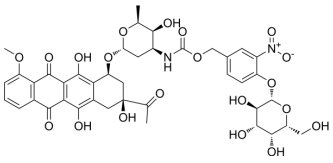
Molecular Weight: 884.79

Target: Topoisomerase; ADC Cytotoxin

Pathway: Cell Cycle/DNA Damage; Antibody-drug Conjugate/ADC Related

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 : ≥ 100 mg/mL (113.02 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.1302 mL	5.6511 mL	11.3021 mL
5 mM	0.2260 mL	1.1302 mL	2.2604 mL
10 mM	0.1130 mL	0.5651 mL	1.1302 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 (2.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Daun02 is a proagent of the topoisomerase inhibitor Daunorubicin.

IC_{50} & Target		
	Topoisomerase	Daunorubicins/Doxorubicins

In Vitro

Daun02 is a prodrug, which is converted by β-galactosidase to Daunorubicin, which has been shown to reduce calcium ion (Ca^{2+})-dependent action potentials in neuroblastoma cells[1]. Daunorubicin is a topoisomerase inhibitor[2]. Daun02 is a good substrate for β-galactosidase (β-gal). The concentration of Daun02 producing 50% (EC_{50}) decrease in cell viability is 0.5 μM, 1.5 μM, and 3.5 μM for T47-D, Panc02, and MCF-7, respectively[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Daun02 is a good substrate for β-gal with K_m and V_{max} values of 0.37 mM and 8.6 μmol/min/mg protein. At a concentration

	of 10^{-5} M, Daun02 is 79% bound to plasma protein compares to 94% for Daunomycin[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Murine Panc02 cells are maintained as exponentiallygrowing monolayer cultures in DMEM/F12 or RPMI-1640 medium supplemented with 10% FBS, 1% glutamine, penicillin, and streptomycin at 37°C. For cytotoxicity assay, the cells are seeded into 96-well microplates and incubated overnight. Initial experiments indicate that FBS contains low levels of intrinsic β-gal activity as evidenced by the slow conversion of Daun02 to Daunomycin; however, this is not evident for human serum. Therefore, prior to addition of Daun02, the FBS concentration is reduced from 10% to 1% for Panc02 cells. Human serum (10%) is used for the transduced human cell lines. The cells are incubated for 24 h and then MTT is added. Lysis buffer (20% SDS dissolved in 50% DMF) is added 4 h after the addition of MTT and the cells are incubated overnight. The optical density at 570 nm is determined using a BIO-RAD microplate reader. Cytotoxicity is expressed as the concentration of drug or prodrug that produced a 50% (EC_{50}) reduction in cell viability[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Male athymic BALB/c mice (nu/nu genotype, 18-20 g) are used. Daunomycin is administered at a dose of 20 mg/kg in 100 µL normal saline solution into the tail vein. Daun02 is administered intraperitoneallyat a dose of 200 mg/kg in 200 µL vehicle. (This route is selected because the volume of drug solution, 200 µL, is too great for tail vein administration.) Tumor volume is determined bycaliper measurement in two dimensions and converted to tumor mass. Tumor growth is monitored over a period of 30 days or until the tumors has reached a mass of 5% of bodyweight (about 1 g). The animals are then killed bycarbon dioxide asphyxiation. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Rep. 2017 Jan 3;7:39817.
- Addict Biol. 2024 May;29(5):e13397.
- Addict Biol. 16 February 2022.
- eNeuro. 2021 Jan 15;ENEURO.0373-20.2021.

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REFERENCES

[1]. Koya E, et al. Targeted disruption of cocaine-activated nucleus accumbens neurons prevents context-specific sensitization. Nat Neurosci. 2009 Aug;12(8):1069-73.

[2]. Lehmann M, et al. Activity of topoisomerase inhibitors daunorubicin, idarubicin, and aclarubicin in the Drosophila Somatic Mutation and Recombination Test. Environ Mol Mutagen. 2004;43(4):250-7.

[3]. Farquhar D, et al. Suicide gene therapy using E. coli beta-galactosidase.Cancer Chemother Pharmacol. Cancer Chemother Pharmacol. 2002 Jul;50(1):65-70.

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