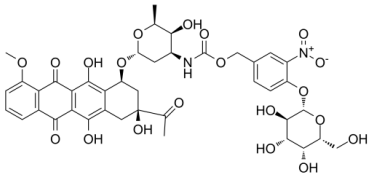
Data Sheet

Product Name:	Daun02
Cat. No.:	CS-0464
CAS No.:	290304-24-4
Molecular Formula:	C41H44N2O20
Molecular Weight:	884.79
Target:	ADC Cytotoxin; Topoisomerase
Pathway:	Antibody-drug Conjugate/ADC Related; Cell Cycle/DNA Damage
Solubility:	DMSO : ≥ 100 mg/mL (113.02 mM)



BIOLOGICAL ACTIVITY:

Daun02 is converted by **β-galactosidase** to Daunorubicin, which is a **topoisomerase** inhibitor. IC50 & Target: Topoisomerase[1][2] **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Daun02 is dissolved in DMSO and stored, and then diluted with appropriate media before use[3].[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]. **Animal Administration:** Daun02 is formulated in normal saline containing 10% DMSO and 10% Emulfur (Mice)[3].[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.

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.

CAIndexNames:

(1R,2R,6S,18R,20S)-3-nitro-4-((2S,3R,4S,5R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yloxy)benzyl (2S,3S,4S,6R)-6-(3-acetyl-3,5,12-trihydroxy-10-methoxy-6,11-dioxo-1,2,3,4,6,11-hexahydrotetracen-1-yloxy)-3-hydroxy-2-methyl-tetrahydro-2H-pyran-4-ylcarbamate

SMILES:

O[C@H]1[C@H](O[C@H]([C@@H]([C@H]1O)O)OC2=CC=C(C=C2[N+]([O-])=O)COC(N[C@@H]3[C@@H]([C@@H](O[C@H](C3)O[C@H]4C[C@](C(C)=O)(CC5=C(C(C(C6=C7C(OC)=CC=C6)=O)=C(C(O)=C54)C7=O)O)O)C)O)=O)CO

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