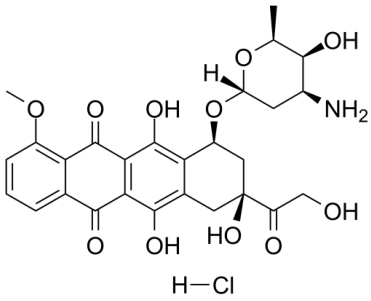
Data Sheet

Product Name:	Doxorubicin (hydrochloride)
Cat. No.:	CS-1239
CAS No.:	25316-40-9
Molecular Formula:	C27H30ClNO11
Molecular Weight:	579.98
Target:	ADC Cytotoxin; AMPK; Apoptosis; Autophagy; HBV; HCV; HIV; Mitophagy; Topoisomerase
Pathway:	Antibody-drug Conjugate/ADC Related; Anti-infection; Apoptosis; Autophagy; Cell Cycle/DNA Damage; Epigenetics; PI3K/Akt/mTOR
Solubility:	DMSO : 50 mg/mL (86.21 mM; Need ultrasonic); H2O : 33.33 mg/mL (57.47 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Doxorubicin hydrochloride (Hydroxydaunorubicin hydrochloride) is a cytotoxic anthracycline antibiotic for the treatment of multiple cancers. The possible mechanisms by which doxorubicin acts in the cancer cell are intercalation into DNA and disruption of **topoisomerase-II**-mediated DNA repair. Doxorubicin hydrochloride reduces basal phosphorylation of **AMPK** and its downstream target acetyl-CoA carboxylase. IC50 & Target: Topoisomerase II[1] **In Vitro:** Combination of Doxorubicin hydrochloride (Hydroxydaunorubicin hydrochloride) and Simvastatin in the highest tested concentrations (2 μM and 10 μM, respectively) kills 97% of the Hela cells[2]. **In Vivo:** Mice bearing PC3 xenografts are injected with 2, 4 or 8 mg/kg Doxorubicin hydrochloride (Hydroxydaunorubicin hydrochloride) and tumor volume is measured over time. A dose of 2 mg/kg does not affect tumor growth while higher dosages delay tumor growth initially ($p<0.05$ at days 18 and 22), 4 mg/kg or 8 mg/kg Doxorubicin significantly reduces levels of c-FLIP in PC3 xenografts[3]. A single intraperitoneal injection 10 mg/kg (Doxorubicin 1) is administered in rats, 10 daily intraperitoneal injections of 1 mg/kg (Doxorubicin 2), or in 5 weekly intraperitoneal injections of 2 mg/kg (Doxorubicin 3). An 80% mortality rate is observed at day 28 in Doxorubicin 1, whereas Doxorubicin 2 and Doxorubicin 3 reached 80% mortality at days 107 and 98, respectively. Fractional shortening decreased by 30% at week 2 in Doxorubicin DOX1, 55% at week 13 in Doxorubicin 2, and 42% at week 13 in Doxorubicin 3[4].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Doxorubicin hydrochloride is dissolved in stock solutions (1 mM) and serially diluted with RPMI 1640 media (0.1, 1, and 2 μM)[2].[2]160 μL of Hela cells suspension (3×10^4 cell/mL) is dispensed into three 96-well U-bottom microplates and incubated for 24 h at 37°C in a fully humidified atmosphere of 5% CO_2. In plate 1, serial dilutions of Doxorubicin (20 μL; final concentration, 0.1-2 μM) and Simvastatin (20 μL; final concentration, 0.25-2 μM) are added to a final volume of 200 μL and incubated for another 72 h. In plates 2 and 3 serial dilutions of each drug (Simvastatin or Doxorubicin, 40 μL) are added. After an incubation period of 24 h, the medium is aspirated and the cells are washed in PBS. Then, serial dilutions of other drug (40 μL) are added and supplemented with culture medium to a final volume of 200 μL, and incubated for 48 h. Doxorubicin and Simvastatin are used individually as positive controls (40 μL in each well), and the cells treated only with solvent are considered as negative controls. To evaluate cell survival, 20 μL of MTT solution (5 mg/mL in PBS) is added to each well and incubated for 3 h. Then the media is replaced with 150 μL of DMSO, and complete solubilization of formazan crystals is achieved by repeated pipetting of the solution. Absorbance is then determined at 540 nm by an ELISA plate reader. Each drug concentration is assayed in 4 or 8 wells and repeated 3 times. The cytotoxic/cytostatic effect of Doxorubicin is expressed as the relative viability (% control) and calculated. Percentage of cell survival in the negative control is assumed as 100. Relative viability=(experimental absorbance-background absorbance)/ (absorbance of untreated controls-background absorbance)×100 %[2]. **Animal Administration:** Doxorubicin is prepared in PBS (containing 0.1% BSA) (Mice)[3].[3][4]Mice [3]

Athymic male nude mice (3-4 weeks old) are used. PC3 cells (4×10^6) are injected subcutaneously into the flanks of mice. Animals

bearing tumors are randomly assigned to treatment groups (five or six mice per group) and treatment initated when xenografts reached volumes of about 100 mm^3. Tumors are measured using digital calipers and volume calculated using the formula: $Volume=Width^2 \times Length \times 0.52$, where width represents the shorter dimension of the tumor. Treatments are administered as indicated using vehicle (PBS containing 0.1% BSA), Doxorubicin (2-8 mg/kg), Apo2L/TRAIL (500 μg/animal), or a combination of 4 mg/kg Doxorubicin followed by 500 μg Apo2L/TRAIL. Doxorubicin is administered systemically whereas Apo2L/TRAIL is given either intra-tumorally or systemically. All treatments are given once. Mice are monitored daily for signs of adverse effects (listlessness and scruffy apparance). Treatments seemed to be well tolerated. The mean±SEM is calculated for each data point. Differences between treatment groups are analyzed by the student t-test. Differences are considered significant when $P<0.05$.

Rats[4]

Thirty male Sprague-Dawley rats weighing 250 to 300 g are randomly assigned to 1 of 3 experimental groups: Doxorubicin schedule 1 (Doxorubicin 1, n=10), Doxorubicin schedule 2 (Doxorubicin 2, n=10), or Doxorubicin schedule 3 (Doxorubicin 3, n=10). For all Doxorubicin treatment schedules, the cumulative dose of Doxorubicin is 10 mg/kg. Schedule 1 involves a single bolus intraperitoneal injection of Doxorubicin at 10 mg/kg. Schedule 2 involves 10 intraperitoneal injections of Doxorubicin at 1 mg/kg for 10 consecutive days. Schedule 3 involves 5 intraperitoneal injections of Doxorubicin at 2 mg/kg, once each week, for 5 wk. Immediately before the first Doxorubicin treatment and at weekly intervals after beginning Doxorubicin treatment, blood pressure and cardiac function are assessed in all surviving animals as long as there are at least 3 rats per group.

References:

[1]. Nitiss JL, et al. Targeting DNA topoisomerase II in cancer chemotherapy.Nat Rev Cancer. 2009 May;9(5):338-50.

[2]. Sadeghi-Aliabadi H, et al. Cytotoxic evaluation of doxorubicin in combination with simvastatin against human cancer cells. Res Pharm Sci. 2010 Jul;5(2):127-33.

[3]. El-Zawahry A, et al. Doxorubicin increases the effectiveness of Apo2L/TRAIL for tumor growth inhibition of prostate cancerxenografts. BMC Cancer. 2005 Jan 7;5:2.

[4]. Hayward R, et al. Doxorubicin cardiotoxicity in the rat: an in vivo characterization. J Am Assoc Lab Anim Sci. 2007 Jul;46(4):20-32.

[5]. Gratia S, et al. Inhibition of AMPK signalling by doxorubicin: at the crossroads of the cardiac responses to energetic, oxidative, and genotoxic stress. Cardiovasc Res. 2012 Aug 1;95(3):290-9.

CAIndexNames:

5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(2-hydroxyacetyl)-1-methoxy-, hydrochloride (1:1), (8S,10S)-

SMILES:

COC1=C2C(C(C(C(O)=C(C[C@](C(CO)=O)(O)C[C@@H]3O[C@@]4([H])C[C@H](N)[C@H](O)[C@H](C)O4)C3=C5O)=C5C2=O)=O)=CC=C1.[H]Cl

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA