Product Data Sheet

Product Name: Doxycycline hyclate
Cat. No.: GC13456

Chemical Properties

Cas. No.	24390-14-5		
Chemical Name	(4S,4aR,5S,5aR,6R,12aR)-4-(dimethylamino)-1,5,10,11,12a-pentahydroxy-6-methyl-3,12-dioxo-3,4,4a,5,5a,6,12,12a-octahydrotetracene-2-carboxamide hydrochloride		
SMILES	O=C(C1=C(O)[C@]2(O)[C@]([C@@H](O)[C@@]3([H])C(C2=O)=C(O)C4=C(O)C=CC=C4[C@@H]3C)([H])[C@H](N(C)C)C1=O)N.Cl		
Formula	$C_{23}H_{29}ClN_2O_9$	M.Wt	512.94
Solubility	≥ 22.15 mg/mL in DMSO, ≥ 49.2 mg/mL in Water with ultrasonic	Storage	4°C, protect from light
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

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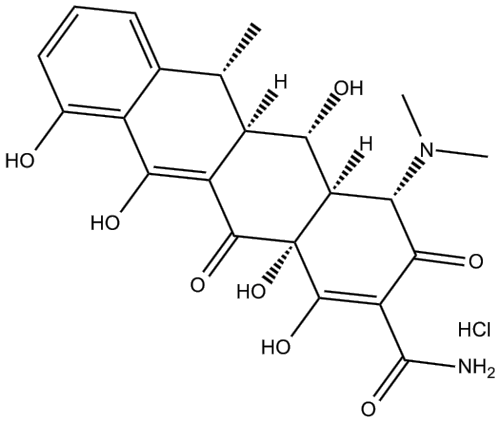
Structure



Protocol

Cell experiment [1]:	
Cell lines	K562 cells (human chronic myeloid leukemia cell line)
Preparation Method	K562 cells were cultured in RPMI 1640 medium supplemented with 10% heat-inactivated fetal bovine serum at 37°C, 5% CO_2, and were treated with Doxycycline hyclate at concentrations 10 to 50μg/ml for 6, 24 and 48 hours, followed by assessment of cell viability, annexin V/propidium iodide staining, Giemsa morphology, mitochondrial membrane potential, cytochrome C release, caspase-2 and caspase-3 activation, γH2AX DNA double strand breaks, Bcl-xL protein level and electrophoretic mobility, and Bcr/Abl tyrosine kinase level; parallel experiments were performed with lysosomal inhibitor chloroquine pretreatment.

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Reaction Conditions	10 to 50μg/ml; 6, 24 and 48h
Applications	Doxycycline hyclate induces exposure-dependent cell death in K562 cells. Doxycycline hyclate dissipates mitochondrial membrane potential and triggers cytochrome C release. Doxycycline hyclate induces DNA double strand breaks and activates caspase-2 at early time points, while caspase-3 activation is a late event. Doxycycline hyclate decreases Bcl-xL protein levels and causes an electrophoretic shift of Bcl-xL molecule. Doxycycline hyclate reduces Bcr/Abl tyrosine kinase levels. Chloroquine restores Bcl-xL and Bcr/Abl protein levels and inhibits caspase-3 activation.
Animal experiment [2]:	
Animal models	Swiss mice infected with *Schistosoma mansoni*
Preparation Method	Mice were infected with *S. mansoni* via subcutaneous injection of 25 cercariae and, after infection confirmation, were treated with Doxycycline hyclate at 5 and 50mg/kg by gavage daily for 60 days; 24 hours after the last treatment, animals were anesthetized and lungs were collected for histopathological and morphometric analysis of granulomas, quantification of eosinophil peroxidase, cytokine levels, iNOS and arginase gene expression, arginase activity, nitric oxide production, lipid/protein oxidation, and immunohistochemical assessment of M1 and M2 macrophage infiltration.
Dosage form	5 and 50mg/kg; p.o.; 60 days

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Applications	Doxycycline hyclate aggravates lung granulomatous inflammation in a dose-dependent manner in *S. mansoni*-infected mice. Doxycycline hyclate increases the number and volume of lung granulomas and shifts granuloma composition toward a productive phenotype. Doxycycline hyclate downregulates IL-4 levels and M2 macrophage recruitment, while upregulating iNOS gene expression, nitric oxide production, IFN-γ, TNF-α, M1 macrophage accumulation, eosinophil peroxidase levels, and tissue protein carbonyl and malondialdehyde levels.

References:

[1] Fares M, Abedi-Valugerdi M, Hassan M, et al. DNA damage, lysosomal degradation and Bcl-xL deamidation in doxycycline- and minocycline-induced cell death in the K562 leukemic cell line. Biochem Biophys Res Commun. 2015 Jul 31;463(3):268-74.

[2] Souza MA, Goncalves-Santos E, Goncalves RV, et al. Doxycycline hyclate stimulates inducible nitric oxide synthase and arginase imbalance, potentiating inflammatory and oxidative lung damage in schistosomiasis. Biomed J. 2022;45(6):857-869.

Background

Doxycycline hyclate is a semi-synthetic tetracycline antibiotic. Doxycycline hyclate binds to the bacterial 30S ribosomal subunit to inhibit protein synthesis and exert bacteriostatic function. Doxycycline hyclate inhibits the expression and activity of matrix metalloproteinases (MMPs). Doxycycline hyclate exerts anti-inflammatory effects by inhibiting neutrophil chemotaxis, lymphocyte proliferation, and release of inflammatory factors. Doxycycline hyclate can be used in studies related to bacterial infections, acne, rosacea, chronic periodontitis, and tumor invasion and metastasis[1-4].

In vitro, treatment of Zmpste24 knockout mouse embryonic fibroblasts and HGPS human skin fibroblasts with Doxycycline hyclate (1μg/mL) for 15 hours alleviated the premature senescence-like phenotype, reduced mRNA and protein expression of IL6 and IL1β, and improved abnormal nuclear envelope morphology[5]. Treatment of human fetal lung fibroblast MRC-5 cells, human large cell lung cancer NCI-H460 cells, and human lung squamous cell carcinoma NCI-H520 cells with Doxycycline

hyclate (10μg/mL) for 24 hours enhanced cell motility and inhibited the migratory ability of cancer cells[6]. Treatment of chronic myeloid leukemia K562 cells with Doxycycline hyclate (10-50μg/mL) for 6-48 hours induced cytotoxicity by causing DNA double-strand breaks and early activation of caspase-2 and late activation of caspase-3[7].

In vivo, oral administration of Doxycycline hyclate (5-50mg/kg) to *Schistosoma mansoni*-infected Swiss mice for 60 days aggravated pulmonary granulomatous inflammation in a dose-dependent manner and increased the number and volume of lung granulomas[8]. A single intravitreal injection of Doxycycline hyclate (5μg/2μL) to ARPE-19 cell-induced proliferative vitreoretinopathy (PVR) C57BL/6J mice reduced the PVR disease score[9]. Intraperitoneal injection of Doxycycline hyclate (40mg/kg) to psychosis-induced Swiss mice for 5 consecutive days improved the deficit in novel object recognition in mice[10].

References:

[1] Cunha BA, Sibley CM, Ristuccia AM. Doxycycline. Ther Drug Monit. 1982;4(2):115-35.

[2] Sloan B, Scheinfeld N. The use and safety of doxycycline hyclate and other second-generation tetracyclines. Expert Opin Drug Saf. 2008 Sep;7(5):571-7.

[3] Xia JL, Wang LQ, Wu LL, et al. Doxycycline hyclate protects lipopolysaccharide-induced endothelial barrier dysfunction by inhibiting the activation of p38 mitogen-activated protein kinase. Biol Pharm Bull. 2014;37(12):1882-90.

[4] Riond JL, Riviere JE. Pharmacology and toxicology of doxycycline. Vet Hum Toxicol. 1988 Oct;30(5):431-43.

[5] Wang M, Zhang J, Qiu J, et al. Doxycycline decelerates aging in progeria mice. Aging Cell. 2024;23:e14188.

[6] Chang HF, Cheng HT, Chen HY, et al. Doxycycline inhibits electric field-induced migration of non-small cell lung cancer(NSCLC) cells. Scientific Reports. 2019 May 30;9:8094.

[7] Fares M, Abedi-Valugerdi M, Hassan M, et al. DNA damage, lysosomal degradation and Bcl-xL deamidation in doxycycline- and minocycline-induced cell death in the K562 leukemic cell line. Biochem Biophys Res Commun. 2015 Jul 31;463(3):268-74.

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[8] Souza MA, Goncalves-Santos E, Goncalves RV, et al. Doxycycline hyclate stimulates inducible nitric oxide synthase and arginase imbalance, potentiating inflammatory and oxidative lung damage in schistosomiasis. Biomed J. 2022;45(6):857-869.

[9] Chen SH, Lin YJ, Wang LC, et al. Doxycycline Ameliorates the Severity of Experimental Proliferative Vitreoretinopathy in Mice. International Journal of Molecular Sciences. 2021 Oct 28;22(21):11670..

[10] Issy AC, Pedrazzi JFC, Oosten ABS van, et al. Effects of doxycycline in Swiss mice predictive models of schizophrenia. Neurotox Res. 2020;38(4):1049-1060.

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