

Product Data Sheet

Product Name: DB1976 hydrochloride

Cat. No.: GC39628

Chemical Properties

Cas. No. 2369663-93-2

SMILES N=C(C1=CC=C2N=C(C3=CC=C(C4=NC5=CC=C(C(N)=N)C=C5N4)[Se]3)NC2=C1)N.[H]Cl.[H]Cl

Formula $C_{20}H_{18}Cl_2N_8Se$ M.Wt 520.28

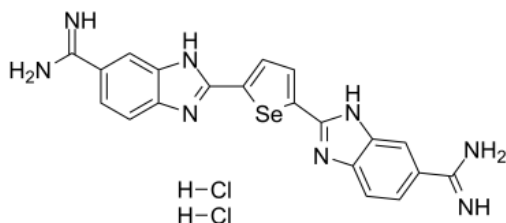
Solubility DMSO : 62.5 mg/mL (120.13 mM; Need ultrason); H₂O : 18.33 mg/mL (35.23 mM; Need ultrasonic)

Storage Store at -20°C

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.

Structure



Protocol

Cell experiment [1]:

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell lines	URE ^{-/-} AML cells ; HEK293 cells.
Preparation Method	PU.1 URE ^{+/-} Msh2 ^{-/-} cells were treated with DB1976(0.1-100mM) for 48 hours. HEK293 cells were treated with DB1976(25μM) for 24 hours.
Reaction Conditions	PU.1 URE ^{-/-} AML cells: (0.1-100) mM,48h;PU.1-negative HEK293 cells:25 μM,24h.
Applications	The IC ₅₀ value of DB1976 dihydrochloride in PU.1-negative HEK293 cells is 2.4 μM ; DB1976 dihydrochloride treatment significantly inhibited the growth of PU.1 URE ^{-/-} AML cells (IC ₅₀ of 105 μM), whereas it had less effect on normal hematopoietic cells (IC ₅₀ of 334 μM).

Animal experiment [2]:

Animal models	PU.1 Inhibition Model
Preparation Method	C57BL/6 mice were administered with Ang-II+ DB 1976 (5 mg/day/kg) by intraperitoneal injection once a day for 28 days.
Dosage form	5 mg/day/kg ; 28 days ; ip.
Applications	DB1976 exposure decreased the interstitial, sub-epicardial and perivascular fibrosis induced by Ang-II in the atrial tissue.

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References:

[1].Antony-Debré I, et al. Pharmacological inhibition of the transcription factor PU.1 in leukemia. J Clin Invest. 2017 Dec 1;127(12):4297-4313

[2].Hu J, et al. PU.1 inhibition attenuates atrial fibrosis and atrial fibrillation vulnerability induced by angiotensin-II by reducing TGF- β 1/Smads pathway activation. J Cell Mol Med. 2021 Jul;25(14):6746-6759..

Background

DB1976 hydrochloride is a efficacious transcription factor PU.1 inhibitor. DB1976 dihydrochloride potently inhibits PU.1 binding (IC₅₀ of 10 nM) and strongly inhibits the PU.1/DNA complex (with high DB1976- λ B affinity, KD of 12 nM) in vitro. DB1976 dihydrochloride has apoptosis-inducing effect^[1] [4].

DB1976 hydrochloride(0.1-100 mM, 48h) led to decrease in the growth of PU.1 URE^{-/-} AML cells (IC₅₀: 105 μ M); After DB1976(25uM,24h) treatment, PU.1 was lentivirally expressed in MOLM13 cells, and it was observed that the cytotoxic effects of the compound were rescued and cell viability was increased after treatment with DB1976^[1].

DB1976 hydrochloride (5 mg/kg/day,28days)exposure decreased the interstitial, sub-epicardial and perivascular fibrosis induced by Ang-II in the atrial tissue^[2]. DB1976 (5 mg/kg/day,28days)effectively attenuated Ang-II-induced increase in the number of atrial fibroblasts and reduced the expression of PCNA, α -SMA, SMemb, ED-A fibronectin, and DDR2 in vitro and in vivo^[2]. In an asthma model, DB1976 (1 mg/kg and 2.5 mg/kg, 5 days per week for 3 weeks) increased airway eosinophils and reduced small airway collagen deposition but had no effect on the number of mucus-secreting cells^[3].

References:

[1]. Antony-Debré I, et al. Pharmacological inhibition of the transcription factor PU.1 in leukemia. J Clin Invest. 2017 Dec 1;127(12):4297-4313.

[2]. Hu J, et al. PU.1 inhibition attenuates atrial fibrosis and atrial fibrillation vulnerability induced by

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angiotensin-II by reducing TGF- β 1/Smads pathway activation. J Cell Mol Med. 2021 Jul;25(14):6746-6759.

[3]. Tu, X., Gomez, H.M., Kim, R.Y. et al. Airway and parenchyma transcriptomics in a house dust mite model of experimental asthma. Respir Res 24, 32 (2023).

[4]. Stephens DC, Kim HM, Kumar A, Farahat AA, Boykin DW, Poon GM. Pharmacologic efficacy of PU.1 inhibition by heterocyclic dications: a mechanistic analysis. Nucleic Acids Res. 2016 May 19;44(9):4005-13.

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