Domatinostat

Cat. No.: HY-16012A

CAS No.: 910462-43-0

Molecular Formula: $C_{23}H_{21}N_5O_3S$

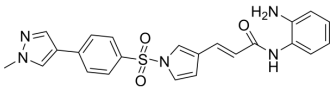
Molecular Weight: 447.51

Target: HDAC; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 58 mg/mL (129.61 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent, Mass	1 mg	5 mg	10 mg
1 mM	2.2346 mL	11.1729 mL	22.3459 mL
5 mM	0.4469 mL	2.2346 mL	4.4692 mL
10 mM	0.2235 mL	1.1173 mL	2.2346 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 (5.59 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Domatinostat (4SC-202 free base) is a selective class I HDAC inhibitor with IC_{50} of 1.20 μM, 1.12 μM, and 0.57 μM for HDAC1, HDAC2, and HDAC3, respectively. It also displays inhibitory activity against Lysine specific demethylase 1 (LSD1).

IC_{50} & Target

HDAC-3 0.57 μM (IC_{50})	HDAC-2 1.12 μM (IC_{50})	HDAC-1 1.2 μM (IC_{50})	HDAC-11 9.7 μM (IC_{50})
HDAC-5 11.3 μM (IC_{50})	HDAC-10 21 μM (IC_{50})	HDAC-9 50 μM (IC_{50})	

In Vitro	Domatinostat (4SC-202 free base) tosylate significantly reduces proliferation of all epithelial and mesenchymal UC cell lines (IC_{50} 0.15-0.51 μM), inhibits clonogenic growth and induces caspase activity[1]. Domatinostat (4SC-202 free base) tosylate provokes apoptosis activation in CRC cells, while caspase inhibitors (z-VAD-CHO and z-DVED-CHO) significantly alleviate Domatinostat (4SC-202 free base) tosylate-exerted cytotoxicity in CRC cells. Meanwhile, Domatinostat (4SC-202 free base) tosylate induces dramatic G2-M arrest in CRC cells. Further studies show that AKT activation might be an important resistance factor of Domatinostat tosylate. Domatinostat (4SC-202 free base) tosylate-induced cytotoxicity is dramatically potentiated with serum starvation, AKT inhibition (by perifosine or MK-2206), or AKT1-shRNA knockdown in CRC cells. On the other hand, exogenous expression of constitutively active AKT1 (CA-AKT1) decreases the sensitivity by Domatinostat tosylate in HT-29 cells. Notably, Domatinostat (4SC-202 free base) tosylate, at a low concentration, enhances oxaliplatin-induced in vitro anti-CRC activity[2]. Domatinostat (4SC-202 free base) tosylate treatment induces potent cytotoxic and proliferation-inhibitory activities against established HCC cell lines (HepG2, HepB3, SMMC-7721) and patient-derived primary HCC cells. Domatinostat (4SC-202 free base) tosylate induces apoptosis signal-regulating kinase 1 (ASK1) activation, causing it translocation to mitochondria and physical association with Cyp-D[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral gavage of Domatinostat (4SC-202 free base) inhibits HT-29 xenograft growth in nude mice, and when combined with oxaliplatin, its activity is further strengthened[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Am J Transl Res. 2020 Jun 15;12(6):2968-2983.

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REFERENCES

[1]. Pinkerneil M, et al. Evaluation of the Therapeutic Potential of the Novel Isotype Specific HDAC Inhibitor 4SC-202 in Urothelial Carcinoma Cell Lines. Target Oncol. 2016 Dec;11(6):783-798.

[2]. Zhijun H, et al. Pre-clinical characterization of 4SC-202, a novel class I HDAC inhibitor, against colorectal cancer cells. Tumour Biol. 2016 Aug;37(8):10257-67.

[3]. Fu M, et al. 4SC-202 activates ASK1-dependent mitochondrial apoptosis pathway to inhibit hepatocellular carcinoma cells. Biochem Biophys Res Commun. 2016 Mar 4;471(2):267-73

[4]. S.W.Henning, et al. Preclinical characterization of 4SC-202, a noval isotype specific HDAC inhibitor.

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