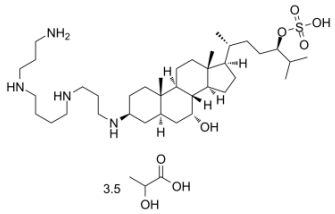
MSI-1436 lactate

Cat. No.:	HY-12219A
CAS No.:	1309370-86-2
Molecular Formula:	$C_{37}H_{72}N_4O_5S \cdot {}_7/_2C_3H_6O_3$
Molecular Weight:	1000.17
Target:	Phosphatase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 54 mg/mL (53.99 mM; Need ultrasonic and warming)

H_2O : ≥ 33.33 mg/mL (33.32 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	0.9998 mL	4.9992 mL	9.9983 mL
5 mM	0.2000 mL	0.9998 mL	1.9997 mL
10 mM	0.1000 mL	0.4999 mL	0.9998 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 3 mg/mL (3.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MSI-1436 lactate is a selective, non-competitive inhibitor of the enzyme protein-tyrosine phosphatase 1B (PTB1B), with an IC_{50} of 1 μM, 200-fold preference over TCPTP (IC_{50} of 224 μM).

IC_{50} & Target

IC50: 1 μM (PTB1B), 224 μM (TCPTP)[1]

In Vitro

MSI-1436's inhibition of TCPTP is approximately two logs less than the effect on PTP1B activity, with a resulting IC_{50} value of 224 μM[1]. MSI-1436 (Trodusquemine, 10 μM) restores ERK phosphorylation in response to mGluR1/5 agonist DHPG in F11 neuronal cells. MSI-1436 (10 uM) rescues DHPG-induced holding currents and restores DSI in LMO4KO BLA neurons[2]. MSI-1436 (0.1-100 μM) blocks PTP1B activity[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	MSI-1436 (10 mg/kg, i.p.) causes obesity-dependent body weight, reduces total body fat content and adipocyte size and lipid content of white adipose tissue of mice[1]. MSI-1436 (Trodusquemine) exhibits anxiolytic effect through a restoration of endocannabinoid (eCB) signaling within the amygdala[2]. MSI-1436 (5 mg/kg, i.p.) has an anti-diabetic effect on diabetic mice, and is sufficient to suppress food intake and cause weight loss in CD1 mice[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Quantitation of phosphatase activity is measured using an intact cell assay. Hep G2 cells are pretreated with 10 μM MSI-1436 lactate or sodium orthovanadate (100 μM, postive control) for 10 min at 37 °C, then incubated with 10 μM pNPP (a cell permeable hydrolysable substrate) for 30 min at 37 °C. Samples of the supernatants are spectrophotometrically analyzed at OD405 for hydolyzed pNP, a direct end product of phosphatase activity[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Male AKR/J mice are randomly placed on ad libitum 10, 45, or 60% fat kcal diets. After 14 weeks, mice are randomly assigned to three treatment groups (n=5 to 8 mice/group); MSI-1436 lactate (initial dose of 10 mg/kg with three subsequent weekly doses of 5 mg/kg, intraperitoneally), vehicle (saline, 10 mL/kg, weekly 4×), or pair-fed (PF). PF animals are injected with saline (weekly 4×) and allotted the amount of food consumed daily by MSI-1436 lactate -treated animals. On day 23, mice are anesthetized and euthanized for blood and tissue collection, respectively. Plasma is obtained following centrifugation of blood 14,000 rpm for 10 min at 4°C[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Commun Biol. 2021 Feb 24;4(1):248.

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REFERENCES

[1]. Lantz KA, et al. Inhibition of PTP1B by trodusquemine (MSI-1436) causes fat-specific weight loss in diet-induced obese mice. Obesity (Silver Spring). 2010 Aug;18(8):1516-1523.

[2]. Qin Z, et al. Chronic stress induces anxiety via an amygdalar intracellular cascade that impairs endocannabinoid signaling. Neuron. 2015 Mar 18;85(6):1319-31.

[3]. Qin Z, et al. Functional properties of Claramine: a novel PTP1B inhibitor and mimetic compound. Biochem Biophys Res Commun. 2015 Feb 27;458(1):21-7.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

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