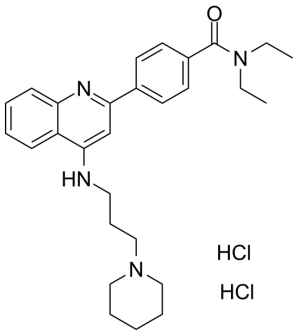
LMPTP inhibitor 1 dihydrochloride

Cat. No.:	HY-111489B
CAS No.:	2310135-46-5
Molecular Formula:	$C_{28}H_{38}Cl_2N_4O$
Molecular Weight:	517.53
Target:	Phosphatase
Pathway:	Metabolic Enzyme/Protease
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 64 mg/mL (123.66 mM)

H_2O : 50 mg/mL (96.61 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9323 mL	9.6613 mL	19.3225 mL
5 mM	0.3865 mL	1.9323 mL	3.8645 mL
10 mM	0.1932 mL	0.9661 mL	1.9323 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (193.23 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LMPTP INHIBITOR 1 (dihydrochloride) is a selective inhibitor of low molecular weight protein tyrosine phosphatase (LMPTP), with an IC_{50} of 0.8 μM LMPTP-A.

IC_{50} & Target

IC50: 0.8 μM (LMPTP-A)[1]

In Vitro	LMPTP INHIBITOR 1 (dihydrochloride) is a selective inhibitor of low molecular weight protein tyrosine phosphatase, with an IC_{50} of 0.8 μM LMPTP-A and shows more potent effect on LMPTP-A versus LMPTP-B. LMPTP inhibitor 1 (Compound 23; 10 μM) also enhances HepG2 IR phosphorylation after insulin stimulation in human HepG2 hepatocytes[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	LMPTP inhibitor 1 is orally bioavailable, and results in appr 680 nM mean serum concentration after treatment of 0.03% w/w, while treatment with 0.05% w/w results in >3 μM; also reverses diabetes in obese mice. LMPTP inhibitor 1 (0.05% w/w) inhibits LMPTP activity, significantly improves glucose tolerance and decreases fasting insulin levels of diabetic DIO mice, without affecting body weight[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Phosphatase assays are performed in buffer containing 50 mM Bis-Tris, pH 6.0, 1 mM DTT and 0.01% Triton X-100 at 37°C. For assays conducted with 3-O-methylfluorescein phosphate (OMFP) as substrate, fluorescence is monitored continuously at λ_{ex} = 485 and λ_{em} = 525 nm. For assays conducted with para-nitrophenylphosphate (pNPP) as substrate, the reaction is stopped by addition of 2X reaction volume of 1 M NaOH, and absorbance is measured at 405 nm. IC_{50} values are determined from plots of LMPTP inhibitor 1 concentration versus percentage of enzyme activity. For inhibitor selectivity assays, each PTP is incubated with either 0.4 mM OMFP or 5 mM pNPP in the presence of 40 μM LMPTP inhibitor 1 or DMSO. Equal units of enzyme activity, comparable to the activity of 10 nM human LMPTP-A, are used. For the inhibitor reversibility assay, 50 nM human LMPTP-A is pre-incubated with 10 μM LMPTP inhibitor 1 or DMSO for 5 min. The enzyme is diluted 100X in phosphatase assay buffer containing 0.4 mM OMFP and fluorescence is measured at the indicated time points[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Human HepG2 cells are cultured in Eagle's Minimal Essential Medium (ATCC) containing 10% fetal bovine serum (FBS), 100 U/mL penicillin and 100 μg/mL streptomycin. The absence of Mycoplasma contamination in HepG2 cultures is confirmed using the Lonza MycoAlert Mycoplasma Detection Kit. Cells are treated with 10 μM LMPTP inhibitor 1 in serum-starvation media (0.1% FBS) overnight, following which cells are stimulated with 10 nM bovine insulin for 5 min at 37°C. For detection of IR tyrosine phosphorylation by immunoprecipitation/Western blotting, cells are lysed in radioimmunoprecipitation assay buffer containing 1 mM phenylmethylsulfonyl fluoride, 10 μg/mL aprotinin/leupeptin, 10 mM sodium orthovanadate, 5 mM sodium fluoride, and 2 mM sodium pyrophosphate, and the IR is immunoprecipitated using the anti-IRβ Ab. IR tyrosine phosphorylation of immunoprecipitates is determined by Western blotting with the anti-pIR/pIGFR-Y1162/Y1163 Ab[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] LMPTP inhibitor 1 is administered to male B6 or $Acp1^{fl/fl}$ albumin-Cre^{+} DIO mice at 0.05% w/w in high-fat diet (HFD) rodent chow. Control groups consist of male B6 or $Acp1^{fl/fl}$ albumin-Cre^{+} littermate mice administered HFD rodent chow alone. Mice are allowed food and water ad libitum and weighed daily. Randomization is not used in these experiments; rather littermate mice are assigned to treatment or control groups in a manner to maintain similar mean body weights between the 2 groups at the start of the study. Insulin-induced liver IR phosphorylation, IPGTT and fasting insulin levels are assessed after treatment. Diabetic (displaying overnight [13 hr] fasting blood glucose levels ≥140 mg/dL) B6 DIO mice are used in experiments to assess IPGTT and fasting insulin levels[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Stanford SM1, et al. Diabetes reversal by inhibition of the low-molecular-weight tyrosine phosphatase. Nat Chem Biol. 2017 Jun;13(6):624-632.

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

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