LMPTP inhibitor 1 hydrochloride

Cat. No.: HY-111489A

CAS No.: 2310135-38-5

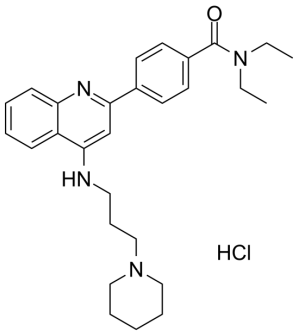
Molecular Formula: $C_{28}H_{37}ClN_4O$

Molecular Weight: 481.07

Target: Phosphatase

Pathway: Metabolic Enzyme/Protease

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	LMPTP inhibitor 1 hydrochloride 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 hydrochloride 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) hydrochloride 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 hydrochloride 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) hydrochloride 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.

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