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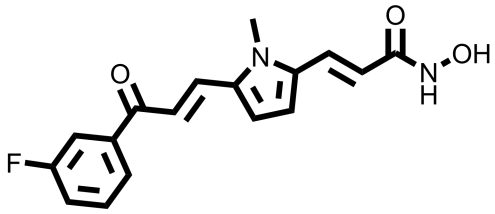
Class IIa HDAC Inhibitor – MC1568

Chemical Name: 3-[5-(3-(3-Fluorophenyl)-3-oxopropen-1-yl)-1-methyl-1H-pyrrol-2-yl]-N-hydroxy-2-propenamide



Molecular Weight:	314.31
Formula:	$C_{17}H_{15}FN_2O_3$
Purity:	≥98%
CAS#:	852475-26-4
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

MC1568 is a potent and selective inhibitor of class IIa histone deacetylases (HDACs), with IC_{50} of 100 nM for maize HD1-A. It is 34-fold more selective for HD1-A than HD1-B, 176-fold more selective for class I HDACs. It exhibits tissue-selective inhibition between members of class II deacetylases in vivo; inhibits HDAC4 and HDAC5 in skeletal muscle and the heart without affecting HDAC3 activity. It arrests myogenesis through the stabilization of myocyte enhancer factor 2D (MEF2D)-HDAC3/4 complex. In a recent study of pancreatic explants, MC1568 enhances expression of Pax4, a key factor required for proper β- and δ-cell differentiation and amplifies endocrine β- and δ-cells.

How to Use:

In vitro: MC1568 was used at 5-10μM final concentration in vitro and cellular assays.

In vivo: MC1568 could be orally dosed to mice at 50 mg/kg once per day (formulation: 0.5% CMC, 5 mg/mL). It has an apparent tissue-selective HDAC inhibition. In skeletal muscle and heart, MC1568 inhibits the activity of HDAC4 and HDAC5 without affecting HDAC3 activity, thereby leaving MEF2-HDAC complexes in a repressed state.

Reference:

1. Mai A, et al. Class II (IIa)-selective histone deacetylase inhibitors. 1. Synthesis and biological evaluation of novel (aryloxopropenyl)pyrrolyl hydroxyamides. (2005) J Med Chem. 48(9):3344-53.
2. Mai A, et al. Identification of two new synthetic histone deacetylase inhibitors that modulate globin gene expression in erythroid cells from healthy donors and patients with thalassemia. (2007) Mol Pharmacol.72(5):1111-23.
3. Duong V, et al. Specific activity of class II histone deacetylases in human breast cancer cells.(2008) Mol Cancer Res.6(12):1908-19.
4. Nebbioso A, et al. Selective class II HDAC inhibitors impair myogenesis by modulating the stability and activity of HDAC-MEF2 complexes. (2009) EMBO Rep. 10(7):776-82.
5. Lenoir O, et al. Specific control of pancreatic endocrine β- and δ-cell mass by class IIa histone deacetylases HDAC4, HDAC5, and HDAC9. (2011) Diabetes. 60(11):2861-71.