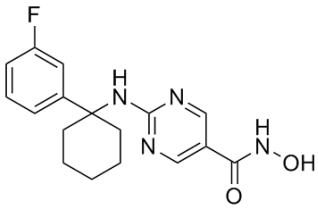
ACY-775

Cat. No.:	HY-19328
CAS No.:	1375466-18-4
Molecular Formula:	$C_{17}H_{19}FN_4O_2$
Molecular Weight:	330.36
Target:	HDAC
Pathway:	Cell Cycle/DNA Damage; Epigenetics
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 : 25 mg/mL (75.68 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0270 mL	15.1350 mL	30.2700 mL
5 mM	0.6054 mL	3.0270 mL	6.0540 mL
10 mM	0.3027 mL	1.5135 mL	3.0270 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 (7.57 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.57 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.57 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ACY-775 is a potent and selective inhibitor of the of histone deacetylase 6 (HDAC6) with an IC_{50} of 7.5 nM.

IC_{50} & Target

HDAC6	HDAC1	HDAC2	HDAC3
7.5 nM (IC_{50})	2123 nM (IC_{50})	2570 nM (IC_{50})	11223 nM (IC_{50})

In Vitro

In vehicle-treated cells, α-tubulin is mainly presented in the deacetylated form, while histone 3 is clearly acetylated. Upon treatment with ACY-775, a clear enhancement of the acetylation of α-tubulin is visible, while histone acetylation remains

	unaltered. Acetylation of α-tubulin is visualized by immunofluorescence and the intensity in the neurites of the neurons is quantified and normalized to the length of the fluorescent signal. In vehicle-treated DRG neurons, acetylated α-tubulin is already present. Upon treatment with ACY-775 the signal intensity of acetylated α-tubulin increases significantly. Significant increase in motility of mitochondria and also the total number of mitochondria within the neurites are observed compare with vehicle-treated DRG neurons. A significantly higher number of retrogradely transport mitochondria is observed in DRG neurons treated with ACY-775 compare with vehicle-treated cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Biodistribution profiles of ACY-738, ACY-775, and tubastatin A are examined after acute dosing at 5 or 50 mg/kg over 2 h. At t=30 min after acute 50 mg/kg injection, respective plasma levels of ACY-738 and ACY-775 are 515 ng/mL (1.9 μM) and 1359 ng/mL (4.1 μM). Elimination from plasma is rapid, with plasmatic half-life of 12 min and concentration below 10 ng/mL after 2 h. Nevertheless, areas under concentration time curves for brain and plasm calculated over 2 h for both ACY-738 and ACY-775 lead to ratios >1. When ACY-738 (5 mg/kg) or ACY-775 (50 mg/kg) are administered repeatedly in wild-type mice at 24 h, 4 h, and 30 min before killing, significant increases in α-tubulin acetylation are observed in all tested brain regions[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Undifferentiated RN46A-B14 cells, a line of immortalized rat raphe neuronal precursors, are grown. They are treated with 2.5 μM ACY-738, ACY-775, tubastatin A, 0.6 μM TSA or vehicle (0.1% DMSO) for 4 h. Samples are processed using histone extraction kit and quantified using protein assay. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice are tested for immobility in the TST. At 30 min or 2 h after i.p. injection of ACY-738 (5, 50 mg/kg), ACY-775 (5, 50 mg/kg), and citalopram (0.5, 2, 20 mg/kg), a combination of the previous, or vehicle, mice are attached to the test rig and time immobile over 6 min is recorded. For open-field activity mice are injected with ACY-738 or ACY-775 at 5, 10, or 50 mg/kg or vehicle and allowed to explore. Activity is recorded[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Dis. 2020 Sep 15;11(9):753.

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REFERENCES

[1]. Veronick Benoy, et al. Development of Improved HDAC6 Inhibitors as Pharmacological Therapy for Axonal Charcot-Marie-Tooth Disease. Neurotherapeutics. 2017 Apr; 14(2): 417-428.

[2]. Jeanine Jochems et al. Antidepressant-Like Properties of Novel HDAC6-Selective Inhibitors with Improved Brain Bioavailability. Neuropsychopharmacology. 2014 Jan; 39(2): 389-400.

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

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