

Product Data Sheet

Product Name: ACY-775

Cat. No.: GC30782

Chemical Properties

Cas. No. 1375466-18-4

SMILES O=C(NO)C(C=N1)=CN=C1NC2(CCCCC2)C3=CC=CC(F)=C3

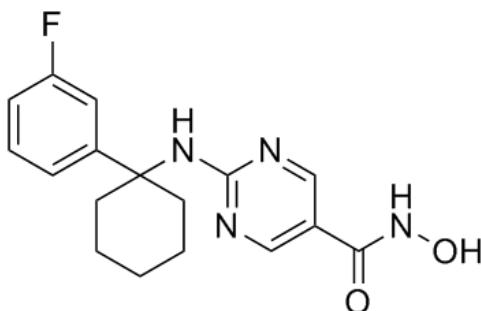
Formula $C_{17}H_{19}FN_4O_2$ M.Wt 330.36

Solubility DMSO : 100 mg/mL (302.70 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment: Undifferentiated RN46A-B14 cells, a line of immortalized rat raphe neuronal precursors, are grown. They are treated with 2.5 μ M ACY-738, ACY-775, tubastatin A, 0.6 μ M TSA or vehicle (0.1% DMSO) for 4 h. Samples are processed using histone extraction kit and quantified using protein assay.

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

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Animal experiment: 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].

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.

Background

ACY-775 is a potent and selective inhibitor of the of histone deacetylase 6 (HDAC6) with an IC₅₀ of 7.5 nM.

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].

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 μ M) and 1359 ng/mL (4.1 μ M). Elimination from plasma is

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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].

[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.

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