

Product Data Sheet

Product Name: Nexturastat A

Cat. No.: GC13764

Chemical Properties

Cas. No. 1403783-31-2

SMILES CCCCN(CC1=CC=C(C=C1)C(=O)NO)C(=O)NC2=CC=CC=C2

Formula $C_{19}H_{23}N_3O_3$

M.Wt 341.4

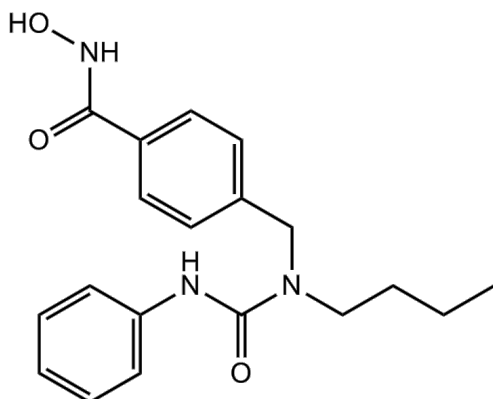
Solubility $\geq 16.3\text{mg/mL}$ in DMSO

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

Kinase experiment [1]:

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

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HDAC inhibition assays

HDAC inhibition assays were performed by Reaction Biology Corp. using isolated human, recombinant full-length HDAC1 and -6 from a baculovirus expression system in Sf9 cells. An acetylated fluorogenic peptide, RHKKAc, derived from residues 379 ~ 382 of p53 was used as substrate. The reaction buffer was made up of 50 mM Tris-HCl pH 8.0, 127 mM NaCl, 2.7 mM KCl, 1 mM MgCl₂, 1 mg/mL BSA, and a final concentration of 1% DMSO. Compounds were delivered in DMSO and delivered to enzyme mixture with preincubation of 5 ~ 10 mins followed by substrate addition and incubation for 2 hrs at 30 °C. Trichostatin A and developer were added to quench the reaction and generate fluorescence, respectively. Dose-response curves were generated starting at 30 µM compound with three-fold serial dilutions to generate a 10-dose plot. IC₅₀ values were then generated from the resulting plots, and the values expressed were the average of duplicate trials ± standard deviation.

Cell experiment [1]:

Cell lines

B16 murine melanoma cells

Preparation method

The solubility of this compound in DMSO is > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.

Reacting condition

100 µM; 48 hrs

Applications

In B16 murine melanoma cells, Nexturastat A dose-dependently elevated acetyl α-tubulin levels without increasing histone H3 acetylation. Moreover, Nexturastat A potently inhibited the growth of B16 melanoma cells, with the GI₅₀ value of 14.3 µM.

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References:

[1]. Bergman JA, Woan K, Perez-Villarroel P, Villagra A, Sotomayor EM, Kozikowski AP. Selective histone deacetylase 6 inhibitors bearing substituted urea linkers inhibit melanoma cell growth. J Med Chem. 2012 Nov 26;55(22):9891-9.

Background

Nexturastat A is a selective inhibitor of histone deacetylase 6 (HDAC6) with IC₅₀ value of 5.2 nM [1].

Nexturastat A is a HDAC inhibitor. It was developed by structural modification of aryl urea HDACIs. The inhibitory activity of Nexturastat A is most potent against HDAC6 with IC₅₀ value of 5.2 nM. Besides that, Nexturastat A also shows inhibition of other HDACs with IC₅₀ values of 3.02, 6.92, 6.68, 9.39, 11.7, 4.46, 0.954, 6.72, 7.57 and 5.14 μ M for HDAC1, 2, 3, 4, 5, 7, 8, 9, 10 and 11, respectively. Nexturastat A has been shown to suppress cell proliferation and promote apoptosis in B16 murine melanoma cells [1, 2].

References:

[1] Kalin J H, Bergman J A. Development and therapeutic implications of selective histone deacetylase 6 inhibitors. Journal of medicinal chemistry, 2013, 56(16): 6297-6313.

[2] Zhang L, Han Y, Jiang Q, et al. Trend of Histone Deacetylase Inhibitors in Cancer Therapy: Isoform Selectivity or Multitargeted Strategy. Medicinal research reviews, 2014.

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