Product Data Sheet

Product Name: AR-42 (OSU-HDAC42)
Cat. No.: GC14590

Chemical Properties

Cas. No.	935881-37-1		
Chemical Name	N-hydroxy-4-[[(2S)-3-methyl-2-phenylbutanoyl]amino]benzamide		
SMILES	CC(C)C(C1=CC=CC=C1)C(=O)NC2=CC=C(C=C2)C(=O)NO		
Formula	$C_{18}H_{20}N_2O_3$	M.Wt	312.36
Solubility	≥ 15.62 mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	AR-42 (OSU-HDAC42)		

Protocol

Kinase experiment [1]:

In vitro HDAC assay	HDAC activity was analyzed by using an HDAC assay kit. This assay was based on the ability of DU-145 nuclear extract, which is rich in HDAC activity, to mediate the deacetylation of the biotinylated [3H]-acetyl histone H4 peptide that was bound to streptavidin agarose beads. The release of [3H]-acetate into the supernatant was measured to calculate the HDAC activity. Sodium butyrate (0.25 ~ 1 mM) was used as a positive control.

Cell experiment [1]:

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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Cell lines	DU-145 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.
Reaction Conditions	10 ~ 1000 nM; 96 hrs
Applications	AR-42 inhibited the growth of DU-145 cells with an IC50 value of 0.11 μM.

Animal experiment [2]:

Animal models	Intact male NCr athymic nude mice inoculated s.c. with PC-3 cells
Dosage form	25 mg/kg, q.d., or 50 mg/kg, q.o.d.; p.o.; for 28 days
Applications	At the doses of 25 mg and 50 mg, AR-42 inhibited the growth of PC-3 tumor xenografts by 52% and 67%, respectively.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Lu Q, Wang DS, Chen CS, Hu YD, Chen CS. Structure-based optimization of phenylbutyrate-derived histone deacetylase inhibitors. J Med Chem. 2005 Aug 25;48(17):5530-5.

[2]. Kulp SK, Chen CS, Wang DS, Chen CY, Chen CS. Antitumor effects of a novel phenylbutyrate-based histone deacetylase inhibitor, (S)-HDAC-42, in prostate cancer. Clin Cancer Res. 2006 Sep 1;12(17):5199-206.

Background

AR-42 (also known as OSU-HDAC42), a derivative of hydroxamate-tethered phenylbutyrate, is a novel and potent inhibitor of histone deacetylase (HDAC) that potently inhibits the activity of HDAC with 50% inhibition concentration IC_{50} value of 16 nM and induces histone H3 acetylation, α-tubulin acetylation and p21 up-regulation, which have been considered as the hallmark indicators of HDAC inhibition. AR-42 has been found to modulate several apoptosis inhibitors as well as cell survival regulator, including Akt, Bcl-xL, Bax, Ku70 and surviving, and exert potent antitumor activity against multiple tumor types, such as human prostate and hepatic cancers, at least partially through PI3K/Akt pathway inhibition.

Reference

[1].Matthew L. Bush†, Janet Oblinger†, Victoria Brendel, Griffin Santarelli, Jie Huang,

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Elena M. Akhmametyeva, Sarah S. Burns, Justin Wheeler, Jeremy Davis, Charles W. Yates, Abhik R. Chaudhury, Samuel Kulp, Ching-Shih Chen, Long-Sheng Chang, D. Bradley Welling, and Abraham Jacob. AR42, a novel histone deacetylase inhibitor, as a potential therapy for vestibular schwannomas and meningiomas. Neuro-Oncology 13(9):983–999, 2011
[2].Aaron M. Sargeant, Robert C. Rengel, Samuel K. Kulp, et al. OSU-HDAC42, a Histone Deacetylase Inhibitor, Blocks Prostate Tumor Progression in the Transgenic Adenocarcinoma of the Mouse Prostate Model Cancer Res 2008;68:3999-4009.
[3].Qiang Lu, Da-Sheng Wang, Chang-Shi Chen, Yuan-Dong Hu, and Ching-Shih Chen. Structure-Based Optimization of Phenylbutyrate-Derived Histone Deacetylase
[4].Inhibitors. J. Med. Chem. 2005, 48, 5530-5535

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