

Product Data Sheet

Product Name: Tubacin
Cat. No.: GC16386

Chemical Properties

Cas. No. 537049-40-4

Chemical Name N-[4-[(2R,4R,6S)-4-[(4,5-diphenyl-1,3-oxazol-2-yl)sulfanylmethyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxyoctanediamide

SMILES C1C(OC(OC1C2=CC=C(C=C2)CO)C3=CC=C(C=C3)NC(=O)CCCCCCC(=O)NO)CSC4=NC(=C(O4)C5=CC=CC=C5)C6=CC=CC=C6

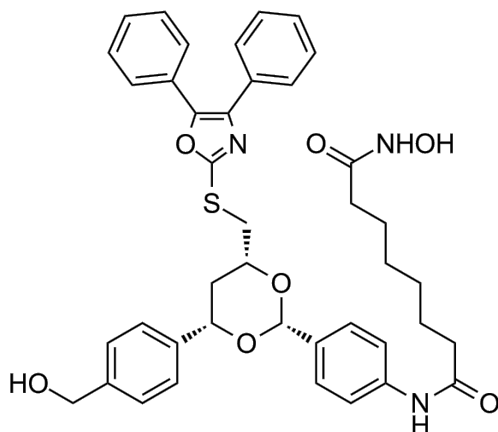
Formula $C_{41}H_{43}N_3O_7S$ M.Wt 721.86

Solubility $\geq 7.19\text{mg/mL}$ 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

Cell experiment [1]:

Cell lines canine renal epithelial cells MDCK.2 cells

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Confluent MDCK.2 cells were split 1:10 in 10-cm dishes. After 24 hours, the cells were again split, resuspended in 10 ml of medium, and pelleted. They were resuspended in 2 ml of medium, and 2×10^4 cells were mixed with growth factor-reduced Matrigel (1.5%) and collagen I (1.5%), MEM (1×), HEPES (20 Preparation Method μM), and NaHCO_3 (0.24%). The Matrigel/collagen I/cell mixture was plated in 24-well plates (450 μl /well) and allowed to solidify for 30 minutes at 37°C before being overlaid with 500 μl of medium. Cells were treated with tubacin, tubastatin-A, or DMSO dissolved in medium on days 0, 2, 4, 6, 8, 10, 12, and 14 after old medium was removed.

Reaction Conditions 10 μM for 0-14 d

Applications Treated the cells with tubacin on days 0, 2, 4, 6, 8, 10, 12, and 14, and this treatment did indeed prevent cyst formation. treated the cells only once with tubacin, on day 0, this single treatment alone slowed the cyst growth.

Animal experiment [2]:

Animal models Colitis models

Preparation Method Freshly prepared 4% (wt/vol) dextran sodium sulfate (DSS) was added daily for 5 days to the pH-balanced tap water of WT B6 mice. Mice were treated daily for 7 days with tubacin or niltubacin (0.5 mg/kg of body weight/day, i.p.), and colitis was assessed by daily monitoring of body weight, stool consistency, and fecal blood. Stool consistency was scored as 0 (hard), 2 (soft), or 4 (diarrhea), and fecal blood (Hemoccult) was scored as 0 (absent), 2 (occult), or 4 (gross).

Dosage form Intraperitoneal injection, 0.5 mg/kg/day

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Applications Tubacin-treated mice were protected against development of weight loss and diarrhea, and this effect was Treg dependent.

References:

- [1]: Cebotaru L, Liu Q, Yanda M K, et al. Inhibition of histone deacetylase 6 activity reduces cyst growth in polycystic kidney disease[J]. Kidney international, 2016, 90(1): 90-99.
- [2]: de Zoeten E F, Wang L, Butler K, et al. Histone deacetylase 6 and heat shock protein 90 control the functions of Foxp3+ T-regulatory cells[J]. Molecular and cellular biology, 2011, 31(10): 2066-2078.

Background

Tubacin (tubulin acetylation inducer) is a small molecule that selectively inhibits histone deacetylase 6 (HDAC6) and induces acetylation of α -tubulin with IC₅₀ of 0.004 μ M [1,2]. Tubacin also inhibited HDAC1 with IC₅₀ of 1.4 μ M [2].

Tubacin preferentially induced α -tubulin hyperacetylation at 2.5 μ M in BMSCs. Tubacin induces α -tubulin acetylation at 5 μ M and protects prostate cancer (LNCaP) cells from hydrogen peroxide-induced death at 8 μ M via peroxiredoxin acetylation [2]. Tubacin (0.25 μ M and 0.5 μ M) with a low concentration could promote BMSC adhesion, proliferation and migration, and tubacin can upregulate the protein levels of VCAM-1, ICAM-1, p-ERK, and acetylated α -tubulin [3]. Incubation with tubacin for 24 h increased the amount of Tumor-derived extracellular vesicles (EVs) in the conditioned media of both FEMX-I and Caco-2 cells by 6.6- and 2.1-fold, respectively [4]. Tubacin significantly altered the cellular lipid composition, which could promote release of CD133+ EVs in FEMX-1 and Caco-2 cells [4].

Tubacin (5 mg/kg, i.p.) significantly increased both mRNA and protein levels for eNOS in the aorta of mice, in the presence of NO donor sodium nitroprusside, tubacin's effects on Ach-mediated vasorelaxation were largely abolished [5]. Pretreatment with tubacin (5 mg/kg, i.p.) significantly reduced cerebral infarct size and the severity of cortical edema at 24 h after arterial occlusion [5]. Tubacin (5 mg/kg) administration significantly reduced the kidney growth in a very aggressive murine model of polycystic kidney disease (PKD) that features the development of giant polycystic kidneys at 3 weeks of age [6].

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- [1]. Aldana-Masangkay G I, Rodriguez-Gonzalez A, Lin T, et al. Tubacin suppresses proliferation and induces apoptosis of acute lymphoblastic leukemia cells[J]. Leukemia & lymphoma, 2011, 52(8): 1544-1555.
- [2]. Butler K V, Kalin J, Brochier C, et al. Rational design and simple chemistry yield a superior, neuroprotective HDAC6 inhibitor, tubastatin A[J]. Journal of the American Chemical Society, 2010, 132(31): 10842-10846.
- [3]. Liang J Q, Lu F, Gan B, et al. Low-dose tubacin promotes BMSCs proliferation and morphological changes through the ERK pathway[J]. American Journal of Translational Research, 2019, 11(3): 1446.
- [4]. Chao O S, Chang T C, Di Bella M A, et al. The HDAC6 inhibitor tubacin induces release of CD133+ extracellular vesicles from cancer cells[J]. Journal of Cellular Biochemistry, 2017, 118(12): 4414-4424.
- [5]. Chen J, Zhang J, Shaik N F, et al. The histone deacetylase inhibitor tubacin mitigates endothelial dysfunction by up-regulating the expression of endothelial nitric oxide synthase[J]. Journal of Biological Chemistry, 2019, 294(51): 19565-19576.
- [6]. Cebotaru L, Liu Q, Yanda M K, et al. Inhibition of histone deacetylase 6 activity reduces cyst growth in polycystic kidney disease[J]. Kidney international, 2016, 90(1): 90-99.

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