Valproic acid

Cat. No.: HY-10585

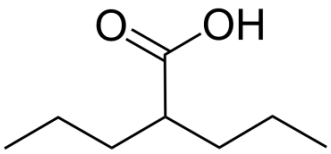
CAS No.: 99-66-1

Molecular Formula: $C_8H_{16}O_2$

Molecular Weight: 144.21

Target: HDAC; Autophagy; Mitophagy; HIV; Notch

Pathway: Cell Cycle/DNA Damage; Epigenetics; Autophagy; Anti-infection; Neuronal Signaling; Stem Cell/Wnt



Storage:

Pure form	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month

SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (693.43 mM; Need ultrasonic)

H_2O : 1 mg/mL (6.93 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	6.9343 mL	34.6717 mL	69.3433 mL
	5 mM	1.3869 mL	6.9343 mL	13.8687 mL
	10 mM	0.6934 mL	3.4672 mL	6.9343 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 (17.34 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (17.34 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (17.34 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Valproic acid (VPA; 2-Propylpentanoic Acid) is an HDAC inhibitor, with IC_{50} in the range of 0.5 and 2 mM, also inhibits HDAC1 (IC_{50}, 400 μM), and induces proteasomal degradation of HDAC2. Valproic acid activates Notch1 signaling and inhibits proliferation in small cell lung cancer (SCLC) cells. Valproic acid sodium salt is used in the treatment of epilepsy, bipolar disorder and prevention of migraine headaches.

IC_{50} & Target	HDAC1 400 μM (IC_{50})	HDAC 0.5-2 mM (IC_{50})	HDAC2	Autophagy
	Mitophagy			
In Vitro	Valproic acid (VPA; 2-Propylpentanoic Acid) inhibits the growth dose- and time-dependently with an IC_{50} of appr 10 and 4 mM at 24 and 72 h, respectively. Valproic acid significantly attenuates the activities of total, cytosol and nuclear HDACs. Valproic acid increases the form of acetylated histone 3 in HeLa cells. Valproic acid (1-3 mM) induces a G1 phase arrest, while 10 mM Valproic acid significantly induces a G2/M phase arrest of cell cycle in HeLa cells. In addition, Valproic acid increases the percentage of sub-G1 cells in HeLa cells in a dose-dependent manner at 24 h[1]. Valproic acid inhibits the mRNA and protein expression of VEGF, VEGFR2 and bFGF. Valproic acid inhibits the protein expression of HDAC1, increases histone H3 acetylation, and enhances the accumulation of hyperacetylated histone H3 on VEGF promoters[2]. Valproic acid treatment results in increased levels of phosphorylated AMPK/ACC in primary mouse hepatocytes. Phosphorylation of ACC following Valproic acid treatment is AMPK-dependent. Valproic acid inhibits the deacetylase activity of both mouse liver nuclear extracts and human recombinant HDAC1 while of the metabolites of Valproic acid, only 2-ene-Valproic acid and 4-ene-Valproic acid diminish deacetylase activity[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			
In Vivo	Valproic acid (VPA; 2-Propylpentanoic Acid; 500 mg/kg, i.p.) inhibits the tumor growth and angiogenesisin the mice transplanted with Kasumi-1 cells. The IR rate in the Valproic acid group is 57.25% at the end of the experiment[2]. Valproic acid (350 mg/kg, i.p.) demonstrates more social investigation and play fighting than control animals[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			

PROTOCOL

Kinase Assay [1]	The activity of caspase-3, -8 and -9 is assessed using the caspase-3, -8 and -9 colorimetric assay kits, respectively. In brief, 1×10^6 cells in a 60-mm culture dish are incubated with 10 mM Valproic acid for 24 h. The cells are then washed in PBS and suspended in 5 volumes of lysis buffer provided with the kit. Protein concentrations are determined using the Bradford method. Supernatants containing 50 μg total protein are used to determine caspase-3, -8 and -9 activities. The supernatants are added to each well in 96-well microtiter plates with DEVD-pNA, IETD-pNA or LEHD-pNA as caspase-3, -8 and -9 substrates and the plates are incubated at 37°C for 1 h. The optical density of each well is measured at 405 nm using a microplate reader. The activity of caspase-3, -8 and -9 is expressed in arbitrary absorbance units. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	In brief, 5×10^5 cells are seeded in 96-well microtiter plates for MTT assays. After exposure to the designated doses of Valproic acid for the indicated times, MTT solution [20 mL: 2 mg/mL in phosphate-buffered saline (PBS)] is added to each well of the 96-well plates. The plates are additionally incubated for 3 h at 37°C. Medium is withdrawn from the plates by pipetting and 200 mL DMSO is added to each well to solubilize the formazan crystals. The optical density is measured at 570 nm using a microplate reader. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Splenectomies are performed on the BALB/c nude mice. One week after the splenectomies, the mice receiv whole body irradiation with 137Cs at a dose of 4 Gy. At 48-72 h post-irradiation, the mice are subcutaneously implanted with Kasumi-1 cells (2×10^7 cells/mouse with 0.15-0.2 mL) in the right axillary region. The mice are randomLy assigned to two groups, the Valproic acid (n=6) and control (n=6) groups. When the tumors are appr 200 mm^3 in size at appr 10 days post-implantation, 0.2 mL Valproic acid (500 mg/kg body weight) or 0.2 mL saline is injected intraperitoneally every day. Valproic acid is dissolved in saline at a concentration of 25 mg/mL. The longest diameter (a) and the shortest diameter (b) of the tumor are measured every three days, and the tumor volume (TV) is calculated according to the following formula: $TV=1/2\times a\times b^2$. Following two weeks of injections, the mice are sacrificed by cervical dislocation and the tumor masses are removed for the following experiments. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biomaterials. 2018 Dec 6;193:30-46.
- EMBO J. 2021 Apr 28;e106771.
- Oncogene. 2021 Mar 12.
- Sci Total Environ. 2021, 147014.
- Acta Pharmacol Sin. 2020 Jun 17.

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[2]. Zhang ZH, et al. Valproic acid inhibits tumor angiogenesis in mice transplanted with Kasumi 1 leukemia cells. Mol Med Rep. 2013 Nov 28.

[3]. Cohen OS, et al. Acute prenatal exposure to a moderate dose of valproic acid increases social behavior and alters gene expression in rats. Int J Dev Neurosci. 2013 Dec;31(8):740-50.

[4]. Avery LB, et al. Valproic Acid Is a Novel Activator of AMP-Activated Protein Kinase and Decreases Liver Mass, Hepatic Fat Accumulation, and Serum Glucose in Obese Mice. Mol Pharmacol. 2014 Jan;85(1):1-10.

[5]. Valproic acid, et al. Histone deacetylase is a direct target of valproic acid, a potent anticonvulsant, mood stabilizer, and teratogen. J Biol Chem. 2001 Sep 28;276(39):36734-41.

[6]. Platta CS, et al. Valproic acid induces Notch1 signaling in small cell lung cancer cells. J Surg Res. 2008 Jul;148(1):31-7.

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