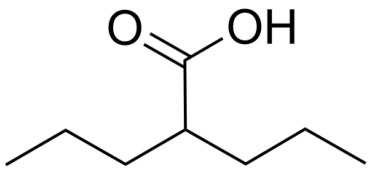
Data Sheet

Product Name:	Valproic acid
Cat. No.:	CS-1765
CAS No.:	99-66-1
Molecular Formula:	$C_8H_{16}O_2$
Molecular Weight:	144.214
Target:	Apoptosis; Autophagy; Endogenous Metabolite; HDAC; HIV; Mitophagy; Notch; Organoid
Pathway:	Anti-infection; Apoptosis; Autophagy; Cell Cycle/DNA Damage; Epigenetics; Metabolic Enzyme/Protease; Neuronal Signaling; Stem Cell/Wnt
Solubility:	DMSO : 100 mg/mL (ultrasonic);H_2O : 1 mg/mL (ultrasonic;warming)



BIOLOGICAL ACTIVITY:

Valproic acid (VPA) is an orally active **HDAC** inhibitor, with **IC_{50}** in the range of 0.5 and 2 mM. Valproic acid 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 is used in the epilepsy, bipolar disorder, metabolic disease, HIV infection and prevention of migraine headaches[1][2][3][4][5][6][7]. IC50 & Target:IC_{50}: 400 μM (HDAC1), 0.5-2 mM (HDAC)[5] HDAC2[6] ***In Vitro:*** Valproic acid (VPA) (0-15 mM; 24 and 72 h) inhibits Hela cell growth in a dose- and time- dependent manner[1].

Valproic acid (10 mM; 24 h) significantly attenuates the activities of total, cytosol and nuclear HDACs[1].

Valproic acid (0-15 mM; 24 h) induces a G1 phase arrest at 1–3 mM and a G2/M phase arrest at 10 mM, and increases the percentage of sub-G1 cells in HeLa cells. Valproic acid also induces necrosis, apoptosis and lactate dehydrogenase (LDH) release[1].

Valproic acid (0-20 mM; 24 h) activates Tcf/Lef-dependent transcription and synergizes with lithium[2].

Valproic acid (0-5 mM; 0-18 h) increases β-catenin levels in Neuro2A cells[2].

Valproic acid (0-2 mM; 0-24 h) stimulates phosphorylation of AMPK and ACC in hepatocytes[5].

Valproic acid (0-10 mM; 2 days) induces Notch1 signaling and morphologic differentiation, suppresses production of NE tumor markers in SCLC cells[6]. ***In Vivo:*** Valproic acid (VPA) (500 mg/kg; i.p.; daily for 12 days) inhibits tumor angiogenesis in mice transplanted with Kasumi-1 cells[3].

Valproic acid (350 mg/kg; i.p.; once) enhances social behavior in rats[4].

Valproic acid (0.26% (w/v); p.o. via drinking water; 14 days) decreases liver mass, hepatic fat accumulation, and serum glucose in obese mice without hepatotoxicity[5].

PROTOCOL (Extracted from published papers and Only for reference)

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. **Cell Assay:** Valproic acid is dissolved in DMSO.[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. **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.

References:

[1]. Han BR, et al. Valproic acid inhibits the growth of HeLa cervical cancer cells via caspase-dependent apoptosis. Oncol Rep. 2013 Dec;30(6):2999-3005.

[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.

[7]. Routy JP, et al. Valproic acid in association with highly active antiretroviral therapy for reducing systemic HIV-1 reservoirs: results from a multicentre randomized clinical study. HIV Med. 2012 May;13(5):291-6.

CAIndexNames:

Pentanoic acid, 2-propyl-

SMILES:

CCCC(CCC)C(O)=O

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

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