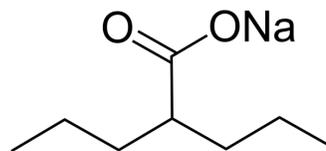


## Valproic acid sodium

|                           |  |
|---------------------------|--|
| <b>Cat. No.:</b>          | HY-10585A  |
| <b>CAS No.:</b>           | 1069-66-5  |
| <b>Molecular Formula:</b> | C <sub>8</sub> H <sub>15</sub> NaO <sub>2</sub>  |
| <b>Molecular Weight:</b>  | 166.19   |
| <b>Target:</b>            | HDAC; Autophagy; Mitophagy; HIV; Notch; Endogenous Metabolite; Apoptosis; Organoid   |
| <b>Pathway:</b>           | Cell Cycle/DNA Damage; Epigenetics; Autophagy; Anti-infection; Neuronal Signaling; Stem Cell/Wnt; Metabolic Enzyme/Protease; Apoptosis |
| <b>Storage:</b>           | 4°C, sealed storage, away from moisture<br>* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)         |



### SOLVENT & SOLUBILITY

|   |  |                          |            |            |
|---|--|--------------------------|------------|------------|
| <b>In Vitro</b>   | H <sub>2</sub> O : 125 mg/mL (752.15 mM; Need ultrasonic)  |                          |            |            |
|   |  | Solvent<br>Concentration | Mass       |            |
|   |  |                          | 1 mg       | 5 mg       |
|   |  |                          | 10 mg      |            |
| <b>Preparing Stock Solutions</b>  | <b>1 mM</b>  | 6.0172 mL                | 30.0860 mL | 60.1721 mL |
|   | <b>5 mM</b>  | 1.2034 mL                | 6.0172 mL  | 12.0344 mL |
|   | <b>10 mM</b>   | 0.6017 mL                | 3.0086 mL  | 6.0172 mL  |
| Please refer to the solubility information to select the appropriate solvent. |  |                          |            |            |
| <b>In Vivo</b>  | 1. Add each solvent one by one: PBS<br>Solubility: 100 mg/mL (601.72 mM); Clear solution; Need ultrasonic<br><br>2. Add each solvent one by one: Saline<br>Solubility: 50 mg/mL (300.86 mM); Clear solution; Need ultrasonic |                          |            |            |

### BIOLOGICAL ACTIVITY

|                                     |   |                                      |       |           |
|-------------------------------------|---|--------------------------------------|-------|-----------|
| <b>Description</b>                  | Valproic acid (Sodium Valproate) sodium is an orally active HDAC inhibitor, with IC <sub>50</sub> in the range of 0.5 and 2 mM, also inhibits HDAC1 (IC <sub>50</sub> , 400 μM), and induces proteasomal degradation of HDAC2. Valproic acid sodium activates Notch1 signaling and inhibits proliferation in small cell lung cancer (SCLC) cells. Valproic acid sodium is used in the treatment of epilepsy, bipolar disorder, metabolic disease, HIV infection and prevention of migraine headaches <sup>[1][2][3][4][5][6][7]</sup> . |                                      |       |           |
| <b>IC<sub>50</sub> &amp; Target</b> | HDAC1<br>400 μM (IC <sub>50</sub> )   | HDAC<br>0.5-2 mM (IC <sub>50</sub> ) | HDAC2 | Autophagy |
|                                     | Mitophagy   |                                      |       |           |

**In Vitro**

Valproic acid (VPA) (0-15 mM; 24 and 72 h) inhibits HeLa cell growth in a dose- and time- dependent manner<sup>[1]</sup>.  
 Valproic acid (10 mM; 24 h) significantly attenuates the activities of total, cytosol and nuclear HDACs<sup>[1]</sup>.  
 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<sup>[1]</sup>.  
 Valproic acid (0-20 mM; 24 h) activates Tcf/Lef-dependent transcription and synergizes with lithium<sup>[2]</sup>.  
 Valproic acid (0-5 mM; 0-18 h) increases  $\beta$ -catenin levels in Neuro2A cells<sup>[2]</sup>.  
 Valproic acid (0-2 mM; 0-24 h) stimulates phosphorylation of AMPK and ACC in hepatocytes<sup>[5]</sup>.  
 Valproic acid (0-10 mM; 2 days) induces Notch1 signaling and morphologic differentiation, suppresses production of NE tumor markers in SCLC cells<sup>[6]</sup>.  
 MCE has not independently confirmed the accuracy of these methods. They are for reference only.  
 Cell Viability Assay<sup>[1]</sup>

|                  |  |
|------------------|--|
| Cell Line:       | HeLa cells   |
| Concentration:   | 0, 1, 3, 5, 10 and 15 mM   |
| Incubation Time: | 24 and 72 h  |
| Result:          | HeLa cell growth was dose- and time-dependently decreased with an IC <sub>50</sub> of ~10 and 4 mM at 24 and 72 h. |

Western Blot Analysis<sup>[1][2][5]</sup>

|                  |  |
|------------------|--|
| Cell Line:       | HeLa cells, Neuro2A cells or primary mouse hepatocytes   |
| Concentration:   | 10 mM (HeLa); 0, 2, and 5 mM (Neuro2A); 0.2, 0.4, 0.8, 1.2 and 2 mM (hepatocytes)  |
| Incubation Time: | 24 h (HeLa); 0-18 h (Neuro2A); 0-24 h (hepatocytes)  |
| Result:          | Increased the form of acetylated histone 3.<br>Reduced PARP, induced cleavage PARP, and downregulated Bcl-2.<br>Increased $\beta$ -catenin levels.<br>Increased the phosphorylation of AMPK and ACC. |

Cell Cycle Analysis<sup>[1]</sup>

|                  |   |
|------------------|---|
| Cell Line:       | HeLa cells  |
| Concentration:   | 0, 1, 3, 5, 10 and 15 mM  |
| Incubation Time: | 24 h  |
| Result:          | Induced a G1 phase arrest at 1–3 mM, significantly induced a G2/M phase arrest at 10 mM, and increased the percentage of sub-G1 cells in HeLa cells in a dose-dependent manner at 24 h. |

**In Vivo**

Valproic acid (VPA) (500 mg/kg; i.p.; daily for 12 days) inhibits tumor angiogenesis in mice transplanted with Kasumi-1 cells<sup>[3]</sup>.  
 Valproic acid (350 mg/kg; i.p.; once) enhances social behavior in rats<sup>[4]</sup>.  
 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<sup>[5]</sup>.  
 MCE has not independently confirmed the accuracy of these methods. They are for reference only.

|               |  |
|---------------|--|
| Animal Model: | Female BALB/c nude mice, Kasumi-1 tumor model <sup>[3]</sup> |
|---------------|--|

|                 |   |
|-----------------|---|
| Dosage:         | 500 mg/kg   |
| Administration: | Intraperitoneal injection, daily for 12 days  |
| Result:         | Inhibited tumor growth and tumor angiogenesis.<br>Inhibited the mRNA and protein expression of VEGF, VEGFR2 and bFGF.<br>Inhibited HDAC activity and increased acetylation of histone H3.<br>Enhanced the accumulation of hyperacetylated histone H3 on VEGF promoters. |
| Animal Model:   | Timed-pregnant Long Evans rats <sup>[4]</sup>   |
| Dosage:         | 350 mg/kg   |
| Administration: | Intraperitoneal injection, once   |
| Result:         | Demonstrated more social investigation and play fighting than control animals.  |
| Animal Model:   | Obese phenotype of ob/ob mice <sup>[5]</sup>  |
| Dosage:         | 0.26% (w/v)   |
| Administration: | Oral via drinking water, 14 days  |
| Result:         | Revealed a marked reduction in the accumulation of fats in the liver as compared with the untreated mice, significantly decreased liver mass to body mass, decreased serum triglyceride concentrations, and did not induce hepatotoxicity.                              |

## CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2024 Jan 22;9(1):24.
- Mil Med Res. 2020 Nov 1;7(1):52.
- Mil Med Res. 2020 Sep 6;7(1):42.
- Adv Sci (Weinh). 2023 Dec 12:e2305620.
- Biomaterials. 2018 Dec 6;193:30-46.

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## REFERENCES

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- [2]. 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.
- [3]. Zhang ZH, et al. Valproic acid inhibits tumor angiogenesis in mice transplanted with Kasumi 1 leukemia cells. *Mol Med Rep.* 2013 Nov 28.
- [4]. 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.
- [5]. 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

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[6]. 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.

[7]. 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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