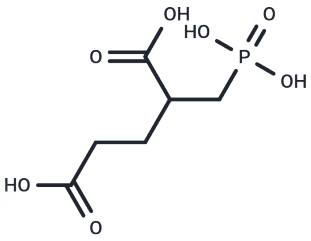
Data Sheet (Cat.No.T3440)

TargetMol

2-PMPA

Chemical Properties



CAS No. : 173039-10-6

Formula: C6H11O7P

Molecular Weight: 226.12

Appearance: no data available

Storage: Pure form: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	2-PMPA (2-(Phosphonomethyl)pentanedioic acid) is a potent and selective inhibitor of glutamate carboxypeptidase II (GCPII) (IC50=300 pM).
Targets(IC50)	Carboxypeptidase
In vitro	2-PMPA acts as a potent, selective inhibitor of the enzyme GCPII, which breaks down the prevalent neuropeptide N-acetyl-aspartyl-glutamate (NAAG) into N-acetylaspartate (NAA) and glutamate. It has shown considerable effectiveness across various animal models of neurological disease. Despite its high polarity and multiple negative charges which pose analytical challenges in biological matrices[1], 2-PMPA notably mitigates the reduction in cell viability and elevation in LDH levels induced by ketamine in mixed cultures, an effect not observed in neuronal cultures[2].
In vivo	Administering 100 mg/kg of 2-PMPA intraperitoneally achieves a peak plasma concentration of 275 μg/mL at 0.25 hours, with pharmacokinetic parameters including a half-life of 0.64 hours, an area under the curve (AUC) of 210 μg×h/mL, an apparent clearance of 7.93 mL/min/kg, and a volume of distribution of 0.44 L/kg[1]. At a dosage of 250 mg/kg in anesthetized mice, 2-PMPA causes an initial increase followed by a rapid decrease and significant attenuation of BOLD signals in gray matter, with its impact on T2* brain signals at dosages of 167 and 250 mg/kg characterized by a notable initial rise lasting several minutes[3]. 2-PMPA shows neuroprotective effects in stroke animal models and anti-allodynic properties in the CCI model. Furthermore, its administration at 50 mg/kg leads to a peak plasma concentration of approximately 29.66±8.1 μM, which is vastly above the threshold needed for inhibiting NAAG peptidase, indicating exceptional brain penetration. This dosage also results in a continuous increase in extracellular NAAG levels starting immediately after administration[4].
Cell Research	Neuronal cultures and neuron-glia mixed cultures are treated with ketamine diluted in the culture medium (1, 3, 10, 30, 100, 300, 1000, 2000, 3000 μM) for 24 h to compare neurotoxicity in these two different cell cultures. 2-PMPA is selected to explore the protective effect on ketamine-induced neurotoxicity in these two different cell cultures. Cells are exposed to 2-PMPA (20, 50, 100 μM) half an hour before 10 μM ketamine treatment in neuronal cultures and 2 mM ketamine treatment in neuron-glia mixed cultures for 24 h. Different doses of ketamine chosen in neuronal cultures and neuron-glia mixed cultures are based on the results of cell viability tests[2].

Solubility Information

Solubility	H2O: 28 mg/mL (123.83 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	4.4224 mL	22.1122 mL	44.2243 mL
5 mM	0.8845 mL	4.4224 mL	8.8449 mL
10 mM	0.4422 mL	2.2112 mL	4.4224 mL
50 mM	0.0884 mL	0.4422 mL	0.8845 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Rais R, et al. Bioanalytical method for evaluating the pharmacokinetics of the GCP-II inhibitor 2-phosphonomethyl pentanedioic acid (2-PMPA). J Pharm Biomed Anal. 2014 Jan;88:162-9.

Zuo D, et al. Existence of glia mitigated ketamine-induced neurotoxicity in neuron-glia mixed cultures of neonatal rat cortex and the glia-mediated protective effect of 2-PMPA. Neurotoxicology. 2014 Sep;44:218-30.

Baslow MH, et al. 2-PMPA, a NAAG peptidase inhibitor, attenuates magnetic resonance BOLD signals in brain of anesthetized mice: evidence of a link between neuron NAAG release and hyperemia. J Mol Neurosci. 2005;26(1):1-15.

Nagel J, et al. Effects of NAAG peptidase inhibitor 2-PMPA in model chronic pain-relation to brain concentration. Neuropharmacology. 2006 Dec;51(7-8):1163-71.