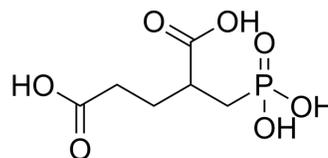


2-PMPA

Cat. No.:	HY-100788
CAS No.:	173039-10-6
Molecular Formula:	C ₆ H ₁₁ O ₇ P
Molecular Weight:	226.12
Target:	Carboxypeptidase
Pathway:	Metabolic Enzyme/Protease
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro	H ₂ O : ≥ 28 mg/mL (123.83 mM) * "≥" means soluble, but saturation unknown.					
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg
			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
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	1. Add each solvent one by one: PBS Solubility: 100 mg/mL (442.24 mM); Clear solution; Need ultrasonic					

BIOLOGICAL ACTIVITY

Description	2-PMPA is a potent and selective inhibitor of glutamate carboxypeptidase II (GCPII) with an IC ₅₀ of 300 pM.
IC ₅₀ & Target	IC ₅₀ : 300 pM (GCPII) ^[1]
In Vitro	2-PMPA is a potent and selective inhibitor of GCPII, an enzyme which catabolizes the abundant neuropeptide N-acetyl-aspartyl-glutamate (NAAG) to N-acetylaspartate (NAA) and glutamate. 2-PMPA demonstrates robust efficacy in numerous animal models of neurological disease. 2-PMPA is a highly polar compound with multiple negative charges causing significant challenges for analysis in biological matrices ^[1] . 2-PMPA reduces ketamine-induced decrease of cell viability and increase of LDH levels in the mixed cultures but not in the neuronal cultures ^[2] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Intraperitoneal administration of 100 mg/kg 2-PMPA results in maximum concentration in plasma of 275 µg/mL at 0.25 h. The half-life, area under the curve, apparent clearance, and volume of distribution are 0.64 h, 210 µg×h/mL, 7.93 mL/min/kg,

and 0.44 L/kg, respectively^[1]. 2-PMPA at 250 mg/kg, in an anesthetized mouse, after an initial rise, produces a rapid decline and a striking attenuation in BOLD signals in gray matter. The signature of 2-PMPA on brain T₂* signals in gray matter at both 167 and 250 mg/kg includes a significant initial rise lasting several minutes^[3]. 2-PMPA has neuroprotective activity in an animal model of stroke and anti-allodynic activity in CCI model. Administration of 2-PMPA (50mg/kg) produces a mean peak concentration of 2-PMPA of 29.66±8.1 μM. This concentration is about 100,000 fold more than is needed for inhibition of NAAG peptidase, and indicates very good penetration to the brain. Administration of 50 mg/kg 2-PMPA (i.p.) produces a continuously increasing extracellular NAAG concentration, which starts directly after application^[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^{[1][3]}

Rats: 2-PMPA is dissolved in methanol and diluted in acetonitrile/water (1:1, v/v). The concentration of stock solution is 1 mg/mL. Male Wistar rats are used in the study. 2-PMPA is administered to male Wistar rats as a single intraperitoneal (i.p.) dose. At 0.08, 0.25, 0.5, 1, 2, and 4 h post dose, blood samples are collected in heparinized microtubes by cardiac puncture immediately before sacrifice. Tissues (brains, sciatic nerves and DRG's) are dissected after exsanguination and immediately flash frozen (-80°C). Plasma is prepared by centrifugation immediately after collection of blood samples. 2-PMPA is assayed in plasma and tissues by the developed LC/MS/MS method^[1].

Mice: Male Swiss-Webster (SW) mice are used in the study. The effect of 2-PMPA is tested on an arbitrarily selected experimental group of 12 mice (group B) by injecting the drug intraperitoneally (i.p.) at 80 mg/kg. The control group (group A) is injected i.p. with the water vehicle. Rotarod tests are then performed at additional times of 70, 240, 420, and 1440 min postinjection, and performance is measured as latency to fall, in seconds, at the tested rpm. A total of 480 2-min Rotarod tests are performed in this experiment^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- ACS Nano. 2021 Apr 27;15(4):7179-7194.
- J Med Chem. 2021 Mar 30.
- Pharmaceuticals. 2023 May 3, 16(5), 692.
- Biochem Biophys Res Commun. 2020 Dec 17;533(4):1393-1399.
- Ghent University. Master of Science in Pharmaceutical Care. 2021 Mar.

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[1]. 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.

[2]. 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.

[3]. 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.

[4]. 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.

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

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