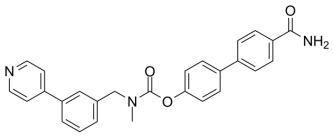
WWL70

Cat. No.:	HY-100337
CAS No.:	947669-91-2
Molecular Formula:	$C_{27}H_{23}N_3O_3$
Molecular Weight:	437.49
Target:	MAGL
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 17.33 mg/mL (39.61 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2858 mL	11.4288 mL	22.8577 mL
	5 mM	0.4572 mL	2.2858 mL	4.5715 mL
	10 mM	0.2286 mL	1.1429 mL	2.2858 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 (5.71 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.2 mg/mL (5.03 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

WWL70 is a selective alpha/beta hydrolase domain 6 (ABHD6) inhibitor with an IC_{50} of 70 nM.

IC_{50} & Target

IC50: 70 nM (ABHD6)[1]

In Vitro

At 1 h after WWL70 (10 μM) treatment, 2-Arachidonoylglycerol (2-AG) is increased by 20% compare to untreated cells. At either 1 or 10 μM, WWL70 completely blocks the lipopolysaccharide (LPS)-induced increase of PGE_2. The enhanced mRNA expression of mPGES-1 and mPGES-2 by LPS is also reduced by WWL70. The IC_{50} of WWL70 to inhibit the PGE_2 biosynthesis is about 100 nM[2].

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

In Vivo	Although post-treatment with WWL70 at 5 mg/kg does not have any effect, treatment with WWL70 at 10 mg/kg improves the performance significantly. WWL70 treatment improves motor coordination of traumatic brain injury (TBI) mice in a concentration dependent manner. The latency to fall in animals treated with WWL70 at 5 mg/kg increases from 74.92±4.8 to 99.57±5.21 on day 3 ($p<0.01$) and from 87.32±4.42 to 100.14±3.56 on day 7 ($p<0.05$) post-injury when compare with the vehicle-TBI groups. At 10 mg/kg, WWL70 treatment improves motor coordination starting on day 1 post-injury. WWL70 treatment completely restores the ability of TBI mice to continuously alternate arms during Y maze exploration (69.67±4.98 %)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	One hundred micrograms per milliliter of BV2 microsomes are pre-incubated with WWL70 for 5 min at 23°C, then mixed with 10 μM of Arachidonic acid (AA) for 1 min at 23°C. 500 μg/mL brain microsomes are incubated with 10 μM of AA for 2 min at 23°C. The reaction is stopped by mixing with stannous acid (5 mg/mL in 0.1 N HCl) to deactivate the enzyme and convert intermediate PGH_2 to $PGF_{2\alpha}$, followed by the measurement of PGE_2 concentration by Enzyme-linked immunoassay (EIA). The activity is determined after subtraction with the amount of PGE_2 in the microsome fraction incubated without substrate [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	BV2 cells (90% confluence) in 10-cm dishes are treated with WWL70 (10 μM) for 1 h. After rinsing with PBS once, the cells are collected by centrifugation at 5000 g for 2 min. The pellet is suspended with 0.1 mL of 0.02% trifluoroacetic acid (TFA) and 1 nmol of 2-AG-d_8 by pipetting and dispersed in 4 mL of acetonitrile in a silanized glass tube to precipitate the debris overnight at -20°C. The supernatant after centrifuged at 5000 g for 5 min is transferred to a new glass tube and evaporated under a nitrogen gas stream in a mild hot water bath (approximately 35°C). 2-AG is resuspended with 0.1 mL of acetonitrile and stored at -80°C until mass analysis[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Seven-week-old, male C57BL/6 mice weighing 25 to 30 g are used in this study. Animals are maintained under a controlled environment with a temperature of 23±2°C, a 12 h light/dark cycle, and access to food and water ad libitum. WWL70 (5 mg/kg or 10 mg/kg) in physiologic saline or an equal volume of 1% DMSO in saline (10 mL/kg) is injected intraperitoneally, and then once a day for 3, 7, or 21 days depending on the experimental design. During the 21-day treatment regimen, animals are subjected to a battery of behavioral tests at different time points. Two hours after the last injection on day 21 post-injury, animals are sacrificed and brain tissues are collected for histological analysis[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Pharmacol Res. 2023 Jul 20;106864.
- Research Square Print. October 14th, 2022.

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REFERENCES

[1]. Li W, et al. A functional proteomic strategy to discover inhibitors for uncharacterized hydrolases. J Am Chem Soc. 2007 Aug 8;129(31):9594-5.

[2]. Tanaka M, et al. WWL70 attenuates PGE2 production derived from 2-arachidonoylglycerol in microglia by ABHD6-independent mechanism. J Neuroinflammation. 2017 Jan 10;14(1):7.

[3]. Tchantchou F, et al. Selective inhibition of alpha/beta-hydrolase domain 6 attenuates neurodegeneration, alleviates blood brain barrier breakdown, and improves functional recovery in a mouse model of traumatic brain injury. J Neurotrauma. 2013 Apr 1;30(7)

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