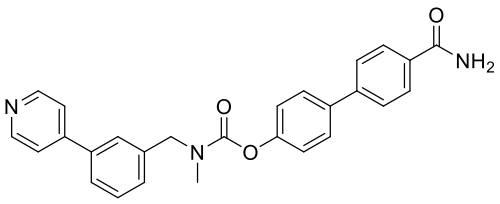
Product data sheet

MedKoo Cat#: 510348 Name: WWL70 CAS#: 947669-91-2 Chemical Formula: $C_{27}H_{23}N_3O_3$ Exact Mass: 437.17394 Molecular Weight: 437.5	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
WWL70 is a potent inhibitor of α/β-hydrolase domain 6 (ABHD6) (IC50 = 70 nM), an enzyme which catalyzes the hydrolysis of 2-arachidonylglycerol.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	7.57	17.30
DMF	2.0	4.57
DMF:PBS (pH 7.2) (1:3)	0.2	0.46

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.29 mL	11.43 mL	22.86 mL
5 mM	0.46 mL	2.29 mL	4.57 mL
10 mM	0.23 mL	1.14 mL	2.29 mL
50 mM	0.05 mL	0.23 mL	0.46 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Tanaka M, Moran S, Wen J, Affram K, Chen T, Symes AJ, Zhang Y. WWL70 attenuates PGE2 production derived from 2-arachidonoylglycerol in microglia by ABHD6-independent mechanism. J Neuroinflammation. 2017 Jan 10;14(1):7. doi: 10.1186/s12974-016-0783-4. PMID: 28086912; PMCID: PMC5234251.

In vivo study

1. Wen J, Jones M, Tanaka M, Selvaraj P, Symes AJ, Cox B, Zhang Y. WWL70 protects against chronic constriction injury-induced neuropathic pain in mice by cannabinoid receptor-independent mechanisms. J Neuroinflammation. 2018 Jan 8;15(1):9. doi: 10.1186/s12974-017-1045-9. PMID: 29310667; PMCID: PMC5759843.
2. Tchantchou F, Zhang Y. 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):565-79. doi: 10.1089/neu.2012.2647. Epub 2013 Apr 5. PMID: 23151067; PMCID: PMC3636589.

7. Bioactivity
Biological target:

Product data sheet

WWL70 is a selective alpha/beta hydrolase domain 6 (ABHD6) inhibitor with an IC50 of 70 nM.

In vitro activity

In this study, WWL70 treatment inhibited 2-AG hydrolysis and increased the intracellular levels of 2-AG. WWL70 also significantly reduced the production of PGE2 in LPS-activated BV2 and primary microglia cells. However, the increased PGE2 production was not affected by another newly developed ABHD6 inhibitor KT182, and the inhibitory effect of WWL70 was also observed in BV2 cells with ABHD6 knockdown. These results suggest that the inhibitory effect of WWL70 on PGE2 production in LPS-activated microglia is not dependent on its inhibition of ABHD6 activity. Treatment with WWL70 reduced the expression of both COX2 and mPGES, the metabolic enzymes crucial for PGE2 production from AA. Furthermore, WWL70 directly inhibited the enzymatic activity of microsomal PGE2 biosynthesis.

Reference: J Neuroinflammation. 2017; 14: 7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5234251/

In vivo activity

The increased activation of microglia and astrocytes in the DRG, sciatic nerve, and dorsal horn of the lumbar spinal cord of the CCI (chronic constriction injury) vehicle group indicates the importance of glial activation in CCI-induced neuropathic pain. Considering the inhibitory effect of WWL70 on microglial activation in previous studies, the possibility of WWL70 in the treatment of neuropathic pain was explored. As anticipated, systemic administration of WWL70 to mice with CCI dramatically reduced microglia and astrocyte activation in the spinal cord dorsal horn and macrophage infiltration in the sciatic nerve and DRG. Moreover, the reduced activation of glial cells by WWL70 treatment after CCI further alleviated the release of pro-nociceptive mediators to facilitate pain relief. These results are consistent with several recent studies indicating spinal microgliosis and macrophage accumulation in DRG and sciatic nerve contribute to pain hypersensitivity after peripheral nerve injury.

Reference: J Neuroinflammation. 2018; 15: 9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5759843/