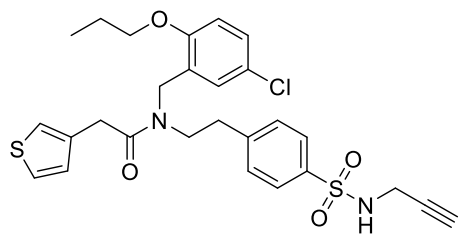
Product data sheet

MedKoo Cat#: 556036 Name: YQ128 CAS#: 2454246-18-3 Chemical Formula: $C_{27}H_{29}ClN_2O_4S_2$ Exact Mass: 544.1257 Molecular Weight: 545.109	
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:
YQ128 is a potent and selective second-generation NLRP3 (NOD-like receptor P3) inflammasome inhibitor with an IC50 of 0.30 ± 0.01 μM. Further studies from in vitro and in vivo models confirmed its selective inhibition on the NLRP3 inflammasome and its brain penetration. Furthermore, pharmacokinetic studies in rats at 20 mg/kg indicated extensive systemic clearance and tissue distribution, leading to a half-life of 6.6 h. However, the oral bioavailability is estimated to be only 10%, which may reflect limited GI permeability and possibly high first-pass effects.

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	175.0	321.04

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.83 mL	9.17 mL	18.34 mL
5 mM	0.37 mL	1.83 mL	3.67 mL
10 mM	0.18 mL	0.92 mL	1.83 mL
50 mM	0.04 mL	0.18 mL	0.37 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. Jiang Y, He L, Green J, Blevins H, Guo C, Patel SH, Halquist MS, McRae M, Venitz J, Wang XY, Zhang S. Discovery of Second-Generation NLRP3 Inflammasome Inhibitors: Design, Synthesis, and Biological Characterization. J Med Chem. 2019 Nov 14;62(21):9718-9731. doi: 10.1021/acs.jmedchem.9b01155. Epub 2019 Oct 31. PMID: 31626545; PMCID: PMC6856409.

In vivo study

1. Jiang Y, He L, Green J, Blevins H, Guo C, Patel SH, Halquist MS, McRae M, Venitz J, Wang XY, Zhang S. Discovery of Second-Generation NLRP3 Inflammasome Inhibitors: Design, Synthesis, and Biological Characterization. J Med Chem. 2019 Nov 14;62(21):9718-9731. doi: 10.1021/acs.jmedchem.9b01155. Epub 2019 Oct 31. PMID: 31626545; PMCID: PMC6856409.

7. Bioactivity
Biological target:

YQ128 is a selective second-generation NLRP3 (NOD-like receptor P3) inflammasome inhibitor with an IC50 of 0.30 μMthat significantly and selectively suppresses the production of IL-1β, but not TNF-α, and it can cross the BBB to reach the CNS.

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In vitro activity

To test whether YQ128 is a brain penetrant, its permeability and transport directionality using immortalized human cerebral microvascular endothelial cells hCMEC/D3 as the human BBB model was determined. This model expresses functional efflux transporters such as P-glycoprotein which are also expressed at the BBB; it has been widely used as a surrogate for human BBB. The potential cytotoxicity of YQ128 on hCMEC/D3 cells was first examined to rule out any potential interference with results interpretation, and the results demonstrated that YQ128 at 20 μM did not show significant toxic effects on these cells. The apical-to-basolateral (A to B) and basolateral-to-apical (B to A) Papp of 17 was 5.21 ± 0.56 × 10−6 and 1.11 ± 0.12 × 10−6 cm/sec, respectively. Thus, YQ128 exhibits an efflux ratio of 0.22, suggesting that YQ128 is not likely subject to active efflux.

Reference: J Med Chem. 2019 Nov 14;62(21):9718-9731. https://pubmed.ncbi.nlm.nih.gov/31626545/

In vivo activity

The in vivo engagement of and selectivity to the NLRP3 inflammasome by YQ128 was tested. C57BL/6 mice (n=4 per group) were pretreated with YQ128 or MCC950 (positive control) at 10 mg/kg before intraperitoneal injection of LPS, which has been shown to trigger IL-1β production in a NLRP3-dependent manner. Serum level of IL-1β was significantly reduced while no significant inhibition on the TNF-α level (Figure 6D) was observed by the treatment of both compounds at the tested dose, thus strongly suggesting the selective in vivo engagement of NLRP3 inflammasome in the observed effects by YQ128 and MCC950. Lastly, the selective inhibition on NLRP3 inflammasome by YQ128 in nlrp3−/− mice (n=3 per group) was confirmed. As expected, upon stimulation with LPS, nlrp3 deficiency abolished the production of IL-1β while the production of TNF-α is normal (Figure 6E). Treatment of nlrp3−/− mice with 17 (10 mg/kg) did not produce inhibition on the level of TNF-α and this again confirmed the selective inhibition on the NLRP3 inflammasome by our compound.

Reference: J Med Chem. 2019 Nov 14;62(21):9718-9731. https://pubmed.ncbi.nlm.nih.gov/31626545/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.