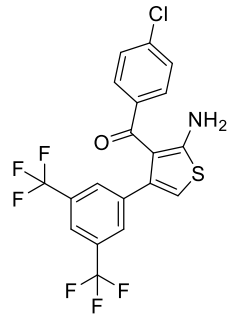
Product data sheet

MedKoo Cat#: 556043 Name: MIPS-521 CAS#: 1146188-19-3 Chemical Formula: $C_{19}H_{10}ClF_6NOS$ Exact Mass: 449.0076 Molecular Weight: 449.7954	
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:
MIPS-521 is a positive allosteric modulator of the A1R that exhibits analgesic efficacy in rats in vivo through modulation of the increased levels of endogenous adenosine that occur in the spinal cord of rats with neuropathic pain. The structure of the A1R is co-bound to adenosine, MIPS521 and a Gi2 heterotrimer, revealing an extrahelical lipid-detergent-facing allosteric binding pocket that involves transmembrane helixes 1, 6 and 7. Molecular dynamics simulations and ligand kinetic binding experiments support a mechanism whereby MIPS521 stabilizes the adenosine-receptor-G protein complex.

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	57.5	127.83

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.22 mL	11.12 mL	22.23 mL
5 mM	0.44 mL	2.22 mL	4.45 mL
10 mM	0.22 mL	1.11 mL	2.22 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Draper-Joyce CJ, Bhola R, Wang J, Bhattarai A, Nguyen ATN, Cowie-Kent I, O'Sullivan K, Chia LY, Venugopal H, Valant C, Thal DM, Wootten D, Panel N, Carlsson J, Christie MJ, White PJ, Scammells P, May LT, Sexton PM, Danev R, Miao Y, Glukhova A, Imlach WL, Christopoulos A. Positive allosteric mechanisms of adenosine A1 receptor-mediated analgesia. Nature. 2021 Sep;597(7877):571-576. doi: 10.1038/s41586-021-03897-2. Epub 2021 Sep 8. PMID: 34497422; PMCID: PMC8711093.

In vivo study

1. Draper-Joyce CJ, Bhola R, Wang J, Bhattarai A, Nguyen ATN, Cowie-Kent I, O'Sullivan K, Chia LY, Venugopal H, Valant C, Thal DM, Wootten D, Panel N, Carlsson J, Christie MJ, White PJ, Scammells P, May LT, Sexton PM, Danev R, Miao Y, Glukhova A, Imlach WL, Christopoulos A. Positive allosteric mechanisms of adenosine A1 receptor-mediated analgesia. Nature. 2021 Sep;597(7877):571-576. doi: 10.1038/s41586-021-03897-2. Epub 2021 Sep 8. PMID: 34497422; PMCID: PMC8711093.

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7. Bioactivity

Biological target:

MIPS521 is a positive allosteric modulator of adenosine A1 receptor (A1AR) that also has a lower A1R allosteric affinity (pKB=4.95; KB=11 μM).

In vitro activity

Relative to VCP171, MIPS521 had lower affinity for the A1R allosteric site (pKB = 4.95 ± 0.40; KB = 11 μM), slightly higher signaling efficacy (Log τB = 0.96 ± 0.34; τ B = 9.12), but substantially higher positive cooperativity (Log αβ = 1.81 ± 0.53; αβ = 64.6) with ADO when assessed in a recombinant cell-based assay of A1R-mediated inhibition of forskolin-stimulated cAMP.

Reference: Nature. 2021 Sep;597(7877):571-576. https://pubmed.ncbi.nlm.nih.gov/34497422/

In vivo activity

To determine whether the cellular effects of VCP171 in spinal cord translated to analgesic efficacy in vivo, mechanical allodynia in nerve-injured rats following direct intrathecal administration of PAM was measured. When tested in vivo, MIPS521 reversed the mechanical hyperalgesia at lower concentrations than VCP171, promoting a robust antinociceptive effect. MIPS521 also significantly reduced spontaneous pain in a conditioned place preference model at a lower dose than VCP171. Encouragingly, MIPS521 had minimal effect on rat atrial beat rate, in contrast to the orthosteric A1R agonist N6-Cyclopentyladenosine (CPA).

Reference: Nature. 2021 Sep;597(7877):571-576. https://pubmed.ncbi.nlm.nih.gov/34497422/