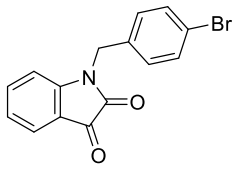
Product data sheet

MedKoo Cat#: 532894 Name: VU0119498 CAS#: 79183-37-2 Chemical Formula: $C_{15}H_{10}BrNO_2$ Exact Mass: 314.9895 Molecular Weight: 316.15	
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:
VU0119498 is a M1 muscarinic receptor agonist (EC50 = 3.1 μM) and pan mAChR M3, M5 positive allosteric modulator (PAM). VU0119498 is a neuroprotective agent.

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	50	158.15

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.16 mL	15.82 mL	31.63 mL
5 mM	0.63 mL	3.16 mL	6.33 mL
10 mM	0.32 mL	1.58 mL	3.16 mL
50 mM	0.06 mL	0.32 mL	0.63 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

Bridges TM, Marlo JE, Niswender CM, Jones CK, Jadhav SB, Gentry PR, Plumley HC, Weaver CD, Conn PJ, Lindsley CW. Discovery of the first highly M5-preferring muscarinic acetylcholine receptor ligand, an M5 positive allosteric modulator derived from a series of 5-trifluoromethoxy N-benzyl isatins. J Med Chem. 2009 Jun 11;52(11):3445-8. doi: 10.1021/jm900286j. PMID: 19438238; PMCID: PMC3875304.

In vivo study

Zhu L, Rossi M, Cohen A, Pham J, Zheng H, Dattaroy D, Mukaibo T, Melvin JE, Langel JL, Hattar S, Matschinsky FM, Appella DH, Doliba NM, Wess J. Allosteric modulation of β-cell M3 muscarinic acetylcholine receptors greatly improves glucose homeostasis in lean and obese mice. Proc Natl Acad Sci U S A. 2019 Sep 10;116(37):18684-18690. doi: 10.1073/pnas.1904943116. Epub 2019 Aug 26. PMID: 31451647; PMCID: PMC6744902.

7. Bioactivity
Biological target:

VU0119498 is a M1 muscarinic receptor agonist (EC50 = 3.1 μM) and pan mAChR M3, M5 positive allosteric modulator (PAM).

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In vitro activity

Functional HTS, identified VU0119498, which displayed micromolar potencies for potentiation of acetylcholine at M1, M3, and M5 receptors in cell-based Ca(2+) mobilization assays. Subsequent optimization led to the discovery of VU0238429, which possessed an EC(50) of approximately 1.16 microM at M5 with >30-fold selectivity versus M1 and M3, with no M2 or M4 potentiator activity.

Reference: Bridges TM, Marlo JE, Niswender CM, Jones CK, Jadhav SB, Gentry PR, Plumley HC, Weaver CD, Conn PJ, Lindsley CW. Discovery of the first highly M5-preferring muscarinic acetylcholine receptor ligand, an M5 positive allosteric modulator derived from a series of 5-trifluoromethoxy N-benzyl isatins. J Med Chem. 2009 Jun 11;52(11):3445-8. doi: 10.1021/jm900286j. PMID: 19438238; PMCID: PMC3875304.

In vivo activity

In this study, VU0119498, a drug known to act as a PAM at M3Rs, significantly augmented ACh-induced insulin release from cultured β cells and mouse and human pancreatic islets. This stimulatory effect was absent in islets prepared from mice lacking M3Rs, indicative of the involvement of M3Rs. VU0119498 treatment of wild-type mice caused a significant increase in plasma insulin levels, accompanied by a striking improvement in glucose tolerance. These effects were mediated by β-cell M3Rs, since they were absent in mutant mice selectively lacking M3Rs in β cells. Moreover, acute VU0119498 treatment of obese, glucose-intolerant mice triggered enhanced insulin release and restored normal glucose tolerance. Interestingly, doses of VU0119498 that led to pronounced improvements in glucose homeostasis did not cause any significant side effects due to activation of M3Rs expressed by other peripheral cell types. Taken together, the data from this proof-of-concept study strongly suggest that M3R PAMs may become clinically useful as novel antidiabetic agents.

Reference: Zhu L, Rossi M, Cohen A, Pham J, Zheng H, Dattaroy D, Mukaibo T, Melvin JE, Langel JL, Hattar S, Matschinsky FM, Appella DH, Doliba NM, Wess J. Allosteric modulation of β-cell M3 muscarinic acetylcholine receptors greatly improves glucose homeostasis in lean and obese mice. Proc Natl Acad Sci U S A. 2019 Sep 10;116(37):18684-18690. doi: 10.1073/pnas.1904943116. Epub 2019 Aug 26. PMID: 31451647; PMCID: PMC6744902.