上海源叶生物科技有限公司
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产品名称：VU0119498
CAS 号： 79183-37-2
产品货号： S89246

生物活性：

Description

VU0119498 是一种泛 Gq mAChR M1，M3，M5 的正变构调节剂 (PAM)，EC50 值分别为 6.04，6.38 和 4.08 μM。VU0119498 具有抗糖尿病活性。

Cellular Effect

Cell Line	Type	Value	Description
CHO	EC_{50}	4.08 μM	Activation of human muscarinic M5 receptor expressed in CHO cells coexpressing Gq protein assessed as potentiation of acetylcholine-induced intracellular Ca2+ mobilization
CHO	EC_{50}	4.1 μM	Agonist activity at human muscarinic M5 expressed in CHO cells assessed as stimulation of calcium mobilization
CHO	EC_{50}	4.6 μM	Positive allosteric modulation of muscarinic M5 receptor expressed in CHO cells assessed as effect on acetylcholine-induced intracellular calcium mobilization after 1 hr by FLIPR assay
CHO	EC_{50}	6.04 μM	Activation of rat muscarinic M1 receptor expressed in CHO cells co-expressing Gq protein assessed as potentiation of acetylcholine-induced intracellular Ca2+ mobilization
CHO	EC_{50}	6.1 μM	Agonist activity at rat muscarinic M1 expressed in CHO cells assessed as stimulation of calcium mobilization
CHO	EC_{50}	6.1 μM	Positive allosteric modulation of muscarinic M1 receptor expressed in CHO cells assessed as effect on acetylcholine-induced intracellular calcium mobilization after 1 hr by FLIPR assay
CHO	EC_{50}	6.38 μM	Activation of human muscarinic M3 receptor expressed in CHO cells coexpressing Gq protein assessed as potentiation of acetylcholine-induced intracellular Ca2+ mobilization
CHO	EC_{50}	6.4 μM	Agonist activity at human muscarinic M3 expressed in CHO cells assessed as stimulation of calcium mobilization
CHO	EC_{50}	6.4 μM	Positive allosteric modulation of muscarinic M3 receptor expressed in CHO cells assessed as effect on acetylcholine-induced intracellular calcium mobilization after 1 hr by FLIPR assay
CHO	EC_{50}	> 30 μM	Agonist activity at rat muscarinic M2 expressed in CHO cells assessed as stimulation of calcium mobilization
CHO	EC_{50}	> 30 μM	Agonist activity at rat muscarinic M4 expressed in CHO cells assessed as stimulation of calcium mobilization

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	CHO	EC_{50}	> 30 μM	Positive allosteric modulation of muscarinic M2 receptor expressed in CHO cells co-expressing Gqi5 assessed as effect on acetylcholine-induced intracellular calcium mobilization after 1 hr by FLIPR assay
	CHO	EC_{50}	> 30 μM	Positive allosteric modulation of muscarinic M4 receptor expressed in CHO cells co-expressing Gqi5 assessed as effect on acetylcholine-induced intracellular calcium mobilization after 1 hr by FLIPR assay

In Vitro

VU0119498 (0.01-30 μM; 150 s) potentiates Ach responses in M1, M3, and M5-expressing CHO cells, with EC50s of 6.04, 6.38, and 4.08 μM, respectively[1].

VU0119498 (3-20 μM) augments ACh-mediated increasing in insulin secretion and intracellular calcium levels in MIN6-K8 cells[3].

VU0119498 (20 μM; 90 min) enhances ACh-induced insulin release in mouse and human pancreatic islets[3].

In Vivo

VU0119498 (0.1-2 mg/kg; a single i.p.) improves glucose tolerance and insulin secretion in mice in a β-cell M3R-dependent fashion[3].

VU0119498 (0.5 mg/kg; a single i.p.) improves glucose tolerance and insulin secretion in obese, glucose-intolerant mice[3].

Animal Model:	Male WT mice (12 weeks)[3]
Dosage:	0.1, 0.5, 2 mg/kg
Administration:	A single i.p.
Result:	Caused a significant improvement in glucose tolerance at the dose of 0.5 mg/kg. Significantly augmented GSIS at the dose of 0.5 mg/kg.

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 : 50 mg/mL (158.15 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.1631 mL	15.8153 mL	31.6306 mL
5 mM	0.6326 mL	3.1631 mL	6.3261 mL
10 mM	0.3163 mL	1.5815 mL	3.1631 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

参考文献

[1]. Bridges TM, et, al. 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.

[2]. Bridges TM, et, al. Chemical lead optimization of a pan Gq mAChR M1, M3, M5 positive allosteric modulator (PAM) lead. Part II: development of a potent and highly selective M1 PAM. Bioorg Med Chem Lett. 2010 Mar 15;20(6):1972-5.

[3]. Zhu L, et, al. Allosteric modulation of β-cell M 3 muscarinic acetylcholine receptors greatly improves

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	glucose homeostasis in lean and obese mice. Proc Natl Acad Sci U S A. 2019 Sep 10;116(37):18684-18690.

完整储备液配制表：

请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80° C, 6 months; -20° C, 1 month。-80° C 储存时，请在 6 个月内使用，-20° C 储存时，请在 1 个月内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	3.1631 mL	15.8153 mL	31.6306 mL	79.0764 mL
	5 mM	0.6326 mL	3.1631 mL	6.3261 mL	15.8153 mL
	10 mM	0.3163 mL	1.5815 mL	3.1631 mL	7.9076 mL
	15 mM	0.2109 mL	1.0544 mL	2.1087 mL	5.2718 mL
	20 mM	0.1582 mL	0.7908 mL	1.5815 mL	3.9538 mL
	25 mM	0.1265 mL	0.6326 mL	1.2652 mL	3.1631 mL
	30 mM	0.1054 mL	0.5272 mL	1.0544 mL	2.6359 mL
	40 mM	0.0791 mL	0.3954 mL	0.7908 mL	1.9769 mL
	50 mM	0.0633 mL	0.3163 mL	0.6326 mL	1.5815 mL
	60 mM	0.0527 mL	0.2636 mL	0.5272 mL	1.3179 mL
	80 mM	0.0395 mL	0.1977 mL	0.3954 mL	0.9885 mL
	100 mM	0.0316 mL	0.1582 mL	0.3163 mL	0.7908 mL