ML380

Cat. No.: HY-12439

CAS No.: 1627138-52-6

Molecular Formula: $C_{23}H_{25}F_3N_4O_3S$

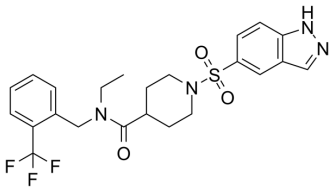
Molecular Weight: 495

Target: mAChR

Pathway: GPCR/G Protein; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (202.02 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0202 mL	10.1010 mL	20.2020 mL
	5 mM	0.4040 mL	2.0202 mL	4.0404 mL
	10 mM	0.2020 mL	1.0101 mL	2.0202 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.05 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.05 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ML380 is a potent, subtype-selective, and brain-penetrant positive allosteric modulator (PAM) of M5 mAChR, with EC_{50}s of 190 and 610 nM for human and rat M5, respectively. ML380 exhibits moderate selectivity versus the M1 and M3 mAChR subtypes. ML380 could increase the affinity of ACh for the M5 mAChR[1][2][3].

IC_{50} & Target

IC50: 190 nM (hM5), 610 nM (rM5)[1]

In Vitro

ML380 (0.01 nM-100 μM) robustly stimulates inositol phosphate (IP) accumulation and Ca^{2+} mobilization in CHO-hM_5 cells,

	with pEC_{50}s of 5.33 and 5.71, respectively[2]. ML380 (0.01-30 μM) increases the ACh-stimulated IP accumulation and Ca^{2+} mobilization in CHO-hM_5 cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ML380 (1 mg/kg; i.v.) displays high clearance (66 mL/min/kg), a moderate volume of distribution (1.6 L/kg), and a short half-life ($t_{1/2}$, 22 min) in rats[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Gentry PR, et, al. Development of a highly potent, novel M5 positive allosteric modulator (PAM) demonstrating CNS exposure: 1-((1H-indazol-5-yl)sulfoneyl)-N-ethyl-N-(2-(trifluoromethyl)benzyl)piperidine-4-carboxamide (ML380). J Med Chem. 2014 Sep 25;57(18

[2]. Berizzi AE, et, al. Molecular Mechanisms of Action of M5 Muscarinic Acetylcholine Receptor Allosteric Modulators. Mol Pharmacol. 2016 Oct;90(4):427-36.

[3]. Berizzi AE, et, al. Structure-Activity Relationships of Pan-Gα q/11 Coupled Muscarinic Acetylcholine Receptor Positive Allosteric Modulators. ACS Chem Neurosci. 2018 Jul 18;9(7):1818-1828.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA