AC260584

Cat. No.: HY-100336

CAS No.: 560083-42-3

Molecular Formula: $C_{20}H_{29}FN_2O_2$

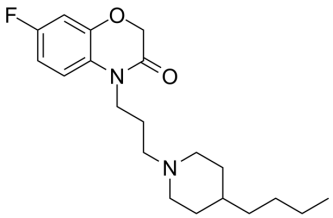
Molecular Weight: 348

Target: mAChR

Pathway: GPCR/G Protein; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (143.68 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	2.8736 mL	14.3678 mL	28.7356 mL
	5 mM	0.5747 mL	2.8736 mL	5.7471 mL
	10 mM	0.2874 mL	1.4368 mL	2.8736 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 (7.18 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.18 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AC260584 is an M1 muscarinic receptor allosteric agonist with a pEC_{50} of 7.6.

IC_{50} & Target

pEC50: 7.6 (M1)[1]

In Vitro

AC260584 is found to be a potent (pEC_{50}=7.6-7.7) and efficacious (90-98% of carbachol) muscarinic M1 receptor agonist. AC260584 shows functional selectivity for the M1 receptor over the M2, M3, M4 and M5 muscarinic receptor subtypes. Its selectivity is found to be similar in native tissues expressing mAChRs to its profile in recombinant systems[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	In rodents, AC260584 activates extracellular signal regulated kinase 1 and 2 (ERK1/2) phosphorylation in the hippocampus, prefrontal cortex and perirhinal cortex. The ERK1/2 activation is dependent upon muscarinic M1 receptor activation since it is not observed in M1 knockout mice. AC260584 also improves the cognitive performance of mice in the novel object recognition assay and its action is blocked by the muscarinic receptor antagonist pirenzepine. In addition, AC260584 is found to be orally bioavailable in rodents[1]. AC260584 at 3 and 10 mg/kg significantly increases dopamine release in the medial prefrontal cortex and hippocampus. However, only the high dose of AC260584, 10 mg/kg (s.c.), significantly increases acetylcholine release in these regions[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats: AC260584 is formulated in 100% 50 mM sodium acetate buffer pH 4.5 at a concentration of 1 mg/mL. Dosing solution is at room temperature prior to dosing. Three rats are administered AC260584 (2 mg/kg) intravenously and three rats are administered the drug orally (10 mg/kg). Rats dosed intravenously are catheterized at the jugular and femoral vein, while those dosed orally are catheterized only at the femoral vein. Rats are housed individually, fasted overnight and dosed by individual body weight. Plasma samples are collected at several time points and analyzed by LC/MS/MS[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Bradley SR, et al. AC260584, an orally bioavailable M(1) muscarinic receptor allosteric agonist, improves cognitive performance in an animal model. Neuropharmacology. 2010 Feb;58(2):365-73.

[2]. Li Z, et al. AC260584 (4-[3-(4-butylpiperidin-1-yl)-propyl]-7-fluoro-4H-benzo[1,4]oxazin-3-one), a selective muscarinic M1 receptor agonist, increases acetylcholine and dopamine release in rat medial prefrontal cortex and hippocampus. Eur J Pharmacol. 200

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