AP521

Cat. No.: HY-100166

CAS No.: 151227-08-6

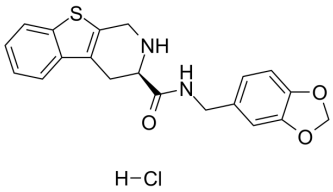
Molecular Formula: $C_{20}H_{19}ClN_2O_3S$

Molecular Weight: 402.89

Target: 5-HT Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (62.05 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
	1 mM	2.4821 mL	12.4103 mL	24.8207 mL
	5 mM	0.4964 mL	2.4821 mL	4.9641 mL
	10 mM	0.2482 mL	1.2410 mL	2.4821 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 (6.21 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AP521 is an agonist of human 5-HT_{1A} receptor with an IC_{50} of 94 nM.

IC_{50} & Target

5-HT_{1A} Receptor 94 nM (IC_{50}, in human)	5-HT_{1A} Receptor 135 nM (IC_{50}, in rat)	5-HT_{1B} Receptor 254 nM (IC_{50}, in rat)	5-HT_{1B} Receptor 5530 nM (IC_{50}, in human)
5-HT_{1D} Receptor 418 nM (IC_{50}, in human)	5-HT_{5A} Receptor 422 nM (IC_{50}, in human)	5-HT_7 Receptor 198 nM (IC_{50}, in rat)	

In Vitro

AP521 is an agonist of human 5-HT_{1A} receptor with IC_{50}s of 135, 94, 254, 5530, 418, 422 and 198 nM for 5-HT_{1A} (rat), 5-HT_{1A} (human), 5-HT_{1B} (rat), 5-HT_{1B} (human), 5-HT_{1D} (human), 5-HT_{5a} (human) and 5-HT_7 (rat), respectively. AP521 also decreases the forskolin-induced cAMP accumulation from 10 nM to 10 μM[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AP521 significantly increases the number of shock acceptances [F(5,105)=4.46, P<0.01] at doses between 0.5 to 10 mg/kg. Oral administration of AP521 at 3 and 10 mg/kg significantly decreases freezing time [F(3,60)=2.89, P<0.05]. AP521 significantly increases the time spent on the open arms by approximately 2-fold as compare to the vehicle treated group [F(3, 36)=4.21, P<0.05 for AP521]. The anxiolytic-like effect of AP521 appears to be dose-related. AP521 significantly increases the extracellular 5-HT level of the medial prefrontal cortex (mPFC) at 10 mg/kg from 0.5 to 1 h after administration. AP521 at 3 mg/kg tends to increase the extracellular 5-HT level, however, this increase is not significant[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Membranes of neurotransmitter receptors are prepared from the tissues of rat, mouse, and guinea pig or from recombinant cells. These membranes are incubated in assay buffers containing selective radioligand for each receptor and AP521. After the incubation, the mixture is vacuum filtered through a glass membrane filter and washed by cold reaction buffer. Afterward, the radioactivity of the filters is counted[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Male Sprague-Dawley rats weighing 250 to 300 g are anesthetized with pentobarbital sodium (50 mg/kg, i.p.) and placed on a stereotaxic apparatus. Dialysis probes with an outer diameter of 0.105 mm are inserted into the guide cannulae so that 3.0 mm of the probes are exposed to the tissue of the medial prefrontal cortex. Rats are housed individually after these operations. On the following day, perfusion is started in the home cage using artificial cerebrospinal fluid (145 mM NaCl, 3.0 mM KCl, 1.3 mM $CaCl_2$, 1.0 mM $MgCl_2$) at a flow rate of 2 mL/min. AP521 (3, 10 mg/kg), tandospirone (10 mg/kg) or vehicle are administered subcutaneously 60 min after sample collection started. The dialysate samples are collected every 30 min for 180 min and extracellular levels of 5-HT are determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Kasahara K, et al. The effects of AP521, a novel anxiolytic drug, in three anxiety models and on serotonergic neural transmission in rats. J Pharmacol Sci. 2015 Jan;127(1):109-16.

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