

LP-211

Chemical Properties

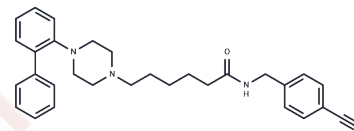
CAS No. : 1052147-86-0

Formula: C₃₀H₃₄N₄O

Molecular Weight: 466.62

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Actual storage temperature shall be subject to the COA.



Biological Description

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| Description | LP-211 is a brain penetrant selective agonist for a 5-HT ₇ receptor (K _i : 0.58 nM), and >300-fold selectivity over the 5-HT _{1A} receptor. |
| Targets(IC ₅₀) | 5-HT Receptor, Dopamine Receptor |
| In vitro | LP-211 showed high 5-HT ₇ receptor affinity (K _i = 0.58 nM), high selectivity over 5-HT _{1A} and D ₂ receptors (324- and 245-fold, respectively), and agonist properties (maximal effect = 82%, EC ₅₀ = 0.60 μM) [1]. Pretreatment with LP-211 had no effect on Fos-like immunoreactivity but strongly increased the response produced by capsaicin [2]. |
| In vivo | After intraperitoneal injection in mice, LP-211 (10 mg/kg) rapidly reached the systemic circulation and entered the brain. Its brain concentration-time profile paralleled that in plasma [1]. SCI rats responded to LP-211 (0.003-0.3, mg/kg, i.v.) with dose-dependent increases in bladder capacity and residual volume [3]. LP-211 reduced synaptic integration in layer 5 pyramidal neurons, which was enhanced in neuropathic pain due to a dysfunction of dendritic hyperpolarization-activated-and-cyclic-nucleotide-regulated (HCN) channels [4]. |
| Kinase Assay | Human 5-HT _{1A} serotonin receptors stably expressed in HEK293 cells were radiolabeled with 1.0 nM [³ H]-8-OH-DPAT. Samples containing 40 μg of membrane protein and different concentrations of each compound ranging from 0.1 nM to 10 μM were incubated in a final volume of 500 μL of 50 mM Tris-HCl pH 7.4, 5 mM MgSO ₄ for 120 min at 37 °C. After this incubation time, samples were filtered through GF/C presoaked in polyethylenimine 0.5% for at least 30 min prior to use. The filters were washed twice with 1 mL of ice-cold buffer (50 mM Tris-HCl, pH 7.4). Nonspecific binding was determined in the presence of 10 μM 5-HT [1]. |
| Animal Research | Mice were given the test compounds intraperitoneally (10 mg/kg) and were killed by decapitation at various times thereafter. Mixed arteriovenous trunk blood was collected in heparinized tubes, centrifuged at 3000g for 10 min, and the plasma was stored at -20 °C. Brain was removed immediately, blotted with paper to remove surface blood, and quickly frozen in dry ice. Compounds and their 1-aryl piperazine metabolites were extracted from plasma and brain homogenate and quantified by reversed-phase HPLC with UV detection (230 nm). Briefly: to 0.1 mL of plasma, 0.2 mL of 20 mM of ammonium bicarbonate and 0.02 mL of a methanolic solution of the internal standard (100 μg/mL) were added; samples were then extracted twice with 1.5 mL of hexane containing 1% of isoamyl alcohol, and the combined extracts were evaporated to dryness and |

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| Animal Research | reconstituted in 0.15 mL of the mobile phase, which was injected into the chromatographic column. Brain tissue was homogenized in distilled water (1 g/10 mL), and 1 mL of the homogenate was extracted twice with 1.5 mL of hexane/isoamyl alcohol as described for plasma. Then, the organic phase was shaken with 0.2 mL of the mobile phase (LP-211 only); after centrifugation, 0.1 mL of the aqueous phase was injected into the chromatographic column [1]. |
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Solubility Information

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| Solubility | DMSO: 90 mg/mL (192.88 mM), Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble) |
| In vivo Formulation | 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (7.07 mM), Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i> |

Preparing Stock Solutions

| | 1mg | 5mg | 10mg |
|-------|-----------|------------|------------|
| 1 mM | 2.1431 mL | 10.7154 mL | 21.4307 mL |
| 5 mM | 0.4286 mL | 2.1431 mL | 4.2861 mL |
| 10 mM | 0.2143 mL | 1.0715 mL | 2.1431 mL |
| 50 mM | 0.0429 mL | 0.2143 mL | 0.4286 mL |

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

- Leopoldo M, et al. Structural modifications of N-(1,2,3,4-tetrahydronaphthalen-1-yl)-4-aryl-1-piperazinehexanamides: influence on lipophilicity and 5-HT₇ receptor activity. Part III. J Med Chem. 2008 Sep 25;51(18):5813-22.
- Martínez-García E, et al. Increase of capsaicin-induced trigeminal Fos-like immunoreactivity by 5-HT₇ receptors. Headache. 2011 Nov-Dec;51(10):1511-9.
- Norouzi-Javidan A, et al. Effect of 5-HT₇ receptor agonist, LP-211, on micturition following spinal cord injury in male rats. Am J Transl Res. 2016 Jun 15;8(6):2525-33. eCollection 2016.
- Santello M, et al. The brain-penetrant 5-HT₇ receptor agonist LP-211 reduces the sensory and affective components of neuropathic pain. Neurobiol Dis. 2017 Oct;106:214-221.

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