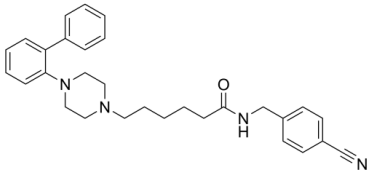
Data Sheet

Product Name:	LP-211
Cat. No.:	CS-0040944
CAS No.:	1052147-86-0
Molecular Formula:	$C_{30}H_{34}N_4O$
Molecular Weight:	466.62
Target:	5-HT Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Solubility:	DMSO : 100 mg/mL (ultrasonic);Ethanol : 50 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

LP-211 is a selective and blood−brain barrier penetrant **5-HT$_7$ receptor** agonist, with a **K_i** of 0.58 nM, with high selectivity over 5-HT $_{1A}$ receptor (K_i, 188 nM) and D_2 receptor (K_i, 142 nM). IC50 & Target: Ki: 0.58 nM (5-HT$_7$ receptor), 188 nM (5-HT$_{1A}$ receptor), 142 nM (D_2 receptor)[1] ***In Vitro:*** LP-211 is a selective 5-HT$_7$ receptor agonist, with a K_i of 0.58 nM, 324- and 245-fold selectivity over 5-HT $_{1A}$ receptor (K_i, 188 nM) and D_2 receptor (K_i, 142 nM). LP-211 shows agonist properties with an EC_{50} of 0.6 μM[1]. ***In Vivo:*** LP-211 (10 mg/kg, i.p.) rapidly reaches the systemic circulation in the mouse, with mean C_{max} of 0.76 ± 0.32 μg/mL at 30 min[1]. LP-211 (0.003-0.3 mg/kg, i.p.) significantly increases the micturition volume in a dose-dependent manner, and causes significant increases in voiding efficiency in spinal cord-injured (SCI) rats, and such effects can be completely reversed by SB-269970[2]. LP-211 (0.25 and 0.50 mg/kg i.p.) improves consolidation of chamber-shape memory in rats, resulting in significant novelty-induced hyperactivity and recognition[3].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Binding of [^{3}H]-LSD at rat cloned **5-HT$_7$ receptor** is performed in the assay. In 1 mL of incubation buffer (50 mM Tris, 10 mM $MgCl_2$ and 0.5 mM EDTA, pH 7.4) are suspended 30 μg of membranes, 2.5 nM [^{3}H]-LSD, **LP-211 (6−9 concentrations)** . The samples are incubated for 60 min at 37°C. The incubation is stopped by rapid filtration on GF/A glass fiber filters (presoaked in 0.5% polyethylenimine for 30 min). The filters are washed with 3 × 53 mL of ice-cold buffer (50 mM Tris, pH 7.4). Nonspecific binding is determined in the presence of 10 μM 5-CT. Approximately 90% of specific binding is determined under these conditions[1].
Animal Administration: LP-211 is formulated in 1% dimethyl sulfoxide (DMSO) in saline (0.9% NaCl)[3].[3]Rats[3]
Thirty male adult Wistar rats (300-450 g) are assessed for novelty preference behavior after acute treatment (administered immediately after the training session and 24 h before the test session). After a 4 weeks' wash out, the rPDT is conducted to evaluate attraction from a greater/uncertain reward, with a sub-chronic treatment (five injections, immediately after sessions which follow the indifferent point). Food restriction, imposed by the experimenter through a limited quantity of food given at the end of each rPDT session, is applied to increase motivation to work for food delivery. All behavioral tests take place between 9:30 am and 4:00 pm. Rats are randomly assigned to treatment (**LP-211 at 0.25 or 0.50 mg/kg i.p.**) and control groups (injection volume 10 mL/kg; n = 10 per group). The brain penetrant 5-HT$_7$R agonist LP-211 is dissolved in a vehicle solution of **1% dimethyl sulfoxide (DMSO) in saline (0.9% NaCl)**. Control group receives the vehicle strictly in the same conditions[3].

References:

[1]. 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.

[2]. 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.

[3]. Beaudet G, et al. LP-211, a selective 5-HT7 receptor agonist, increases novelty-preference and promotes risk-prone behavior in rats. Synapse. 2017 Dec;71(12).

CAIndexNames:

1-Piperazinehexanamide, 4-[1,1'-biphenyl]-2-yl-N-[(4-cyanophenyl)methyl]-

SMILES:

O=C(NCC1=CC=C(C#N)C=C1)CCCCCN2CCN(C3=CC=CC=C3C4=CC=CC=C4)CC2

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