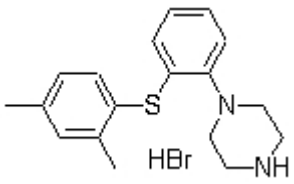
Product Introduction

Vortioxetine (Lu AA21004) HBr

Vortioxetine (Lu AA21004) is a multimodal serotonergic agent, inhibits **5-HT1A**, **5-HT1B**, **5-HT3A**, **5-HT7** receptor and **SERT** with **IC50** of 15 nM, 33 nM, 3.7 nM, 19 nM and 1.6 nM, respectively. Phase 3.

Technical Data:

Molecular Weight (MW):	379.36	
Formula:	$C_{18}H_{22}N_2S.HBr$	
Solubility (25°C) *** <1 mg/ml means slightly soluble or insoluble:**	DMSO 76 mg/mL	
	Water <1 mg/mL	
	Ethanol 17 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	960203-27-4	

Biological Activity

Lu-AA21004 inhibits recombinant human CYP1A2, CYP2C9, CYP2D6 and CYP3A4 with IC50 of 40 μM, 39 μM, 9.8 μM and 10 μM, respectively. [1] Lu AA21004 is a partial h5-HT1B receptor agonist with EC50 of 460 nM and intrinsic activity of 22% using a whole-cell cAMP-based assay. Lu AA21004 binds to the r5-HT7 receptor with a Ki value of 200 nM and is a functional antagonist at the r5-HT7 receptor with an IC50 of 2 μM in an in vitro whole-cell cAMP assay. [2]

For Lu-AA21004 the hepatic clearances and oral bioavailabilities in rats are found to be 7.1 (L/h)/kg and

16%. Lu-AA21004 (2.5 mg/kg, 5 mg/kg, or 10 mg/kg sc) increases the extracellular levels of 5-HT in the ventral hippocampus in conscious rats. Lu-AA21004 (5 mg/kg, or 10 mg/kg sc) also results in significantly higher basal levels of 5-HT in the medial prefrontal cortex (mPFC) after 3 days of treatment. Lu-AA21004 occupies SERT by 43% and 57% after 3 days of treatment with 5 mg/kg or 10 mg/kg in the rat medial prefrontal cortex. [1] Lu AA21004 dose-dependent occupies 5-HT1B receptor and the SERT with ED50 of 3.2 mg/kg and 0.4 mg/kg in rats one hour after subcutaneous administration. Lu AA21004 affects the Bezold-Jarisch reflex in the rat dose dependently, inhibiting transient bradycardia with ED50 of 0.11 mg/kg. Lu AA21004 (2.5-10.0 mg/kg s.c.) increases extracellular levels of 5-HT, DA, and NA in the medial prefrontal cortex and in the ventral hippocampus in rats. Lu AA21004 (5 mg/kg s.c.) increases in the extracellular levels of 5-HT (200%) in the ventral hippocampus of rats with 41% occupancy at the SERT. Lu AA21004 (7.8 mg/kg s.c.) significantly decreases the immobility time in the FSL rats but not in the FRL rats. Lu AA21004 (8.0 mg/kg p.o.) produces an increase in social interaction as well as a small, but significant, increase in locomotor activity in rats. Lu AA21004 (7.9 mg/kg s.c.) shows a dose-dependent anxiolytic-like effect in the conditioned fear assay in rats. [2] Vortioxetine (10 mg/kg) significantly increases freezing 60 min before acquisition in male Sprague-Dawley rats, suggesting enhanced contextual memory formation during acquisition and/or consolidation. Vortioxetine (5 mg/kg) also causes increased freezing rates during retention, an effect that reached statistical significance by post hoc tests. Vortioxetine (2.5 mg/kg or 5 mg/kg) prior to acquisition shows average exploration times of 29s and 33s for the novel object, respectively. Vortioxetine (10 mg/kg) significantly reduces nociception in rats, assessed as increased paw withdrawal latency. Vortioxetine at 5 and 10 mg/kg increases the levels of ACh to 224% and 204% of baseline 20 min after injection. [3]

A multimodal antidepressant.

References

[1] Bang-Andersen B, et al. J Med Chem, 2011, 54(9), 3206-3221.

[2] M?rk A, et al. J Pharmacol Exp Ther, 2012, 340(3), 666-675.

[3] M?rk A, et al. Pharmacol Biochem Behav, 2013, 105C, 41-50.

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