Naluzotan

Cat. No.: HY-14848

CAS No.: 740873-06-7

Molecular Formula: $C_{23}H_{38}N_4O_3S$

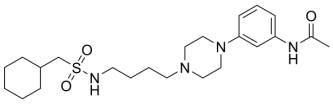
Molecular Weight: 450.64

Target: 5-HT Receptor; Potassium Channel

Pathway: GPCR/G Protein; Neuronal Signaling; Membrane Transporter/Ion Channel

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



BIOLOGICAL ACTIVITY

Description

Naluzotan is a novel, potent, and selective amidosulfonamide 5-HT1A agonist with IC_{50} and K_i of appr 20 nM and 5.1 nM, used for the treatment of anxiety and depression; Also a weak hERG K^+ channel blocker, with IC_{50} of 3800 nM.

IC_{50} & Target

5-HT_{1A} Receptor 20 nM (IC_{50})	5-HT_{1A} Receptor 5.1 nM (Ki)	hERG K^+ channel 3800 nM (IC_{50})

In Vitro

Naluzotan behaves as a full agonist in an in vitro cell-based functional assay with an EC_{50} of 20 nM. Naluzotan has significant affinity is the guinea pig sigma receptor (K_i = 100 nM), but does not inhibit cytochrome P450 isoforms (CYP) 1A2, 2C9, 2C19, 2D6, and 3A4[1].

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

In Vivo

In rats Naluzotan shows 11% oral bioavailability with a serum $t_{1/2}$ of 2−3.5 h when administrated po, attaining a C_{max} level of 24 ± 13 ng/mL (3 mg/kg, po). Naluzotan shows significant brain penetration, achieving a brain:serum concentration ratio of approximately 0.5 in the rat at 1 h following either intravenous or oral administration and reaching brain concentration approximately equivalent to that of buspirone. In dogs the pharmacokinetic profile of naluzotan shows 16% oral bioavailability, a serum $t_{1/2}$ of 1.1 h po, and a C_{max} level of 174 ± 141 ng/mL (3 mg/kg, po)[1]. PRX-00023 (0.01-0.05 mg/kg, i.p.) significantly reduces USV rates, but done of these doses produce sedation in rats[2].

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PROTOCOL

Animal Administration [2]

PRX-00023 and buspirone are used in the assay. Drugs are dissolved in saline vehicle prior to injections. Each pup is injected in the intraperitoneal space (i.p.) with one of several doses of PRX-00023 (0.01, 0.03, 0.05, 0.1, 0.3, 1.0, and 3.0 mg/kg in saline, for a total volume of 0.1 mg/kg). Within each litter two littermates, though occasionally one, receive the same dose of a compound. Because of the distribution of pups in litters used, no Random line pups are tested with PRX-00023 at 3.0 mg/kg for comparison to vehicle.

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

REFERENCES

[1]. Becker OM, et al. An integrated in silico 3D model-driven discovery of a novel, potent, and selective amidosulfonamide 5-HT1A agonist (PRX-00023) for the treatment of anxiety and depression. J Med Chem. 2006 Jun 1;49(11):3116-35.

[2]. Brunelli SA, et al. PRX-00023, a selective serotonin 1A receptor agonist, reduces ultrasonic vocalizations in infant rats bred for high infantile anxiety. Pharmacol Biochem Behav. 2009 Nov;94(1):8-15.

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