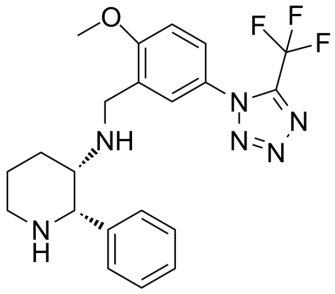
Vofopitant

Cat. No.:	HY-12142
CAS No.:	168266-90-8
Molecular Formula:	$C_{21}H_{23}F_3N_6O$
Molecular Weight:	432.44
Target:	Neurokinin Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



BIOLOGICAL ACTIVITY

Description	Vofopitant is potent tachykinin NK_1 receptor antagonist, with pK_is of 10.6, 9.5, and 9.8 for human, rat and ferret NK_1 receptor, respectively.
IC_{50} & Target	pKi: 10.6 (Human NK_1 receptor), 9.5 (Rat NK_1 receptor), 9.8 (Ferret NK_1 receptor)[1]
In Vitro	Vofopitant is potent tachykinin NK_1 receptor antagonist, with pK_is of 10.6, 9.5, and 9.8 for human, rat and ferret NK_1 receptor, respectively. Vofopitant less potently inhibits rat 5-HT1A, bovine 5-HT1D, rat 5-HT2A, rat Histamine H1, guinea-pig Histamine H2 and rat Ca^{2+} channel, with pK_is of 6.3, 6.6, 6.5, 6.5, 6.6, and 5.6, respectively. Vofopitant shows negligible affinity at NK_2 and NK_3, with pIC_{50} of <5.0[1]. GR205171 (300 μM) potentiates the effects of paroxetine on cortical [5-HT]ext, and inhibits paroxetine-induced increase in [5-HT]ext in the dorsal raphe nucleus[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Vofopitant (GR205171, 30 mg/kg, s.c.) increases the number of choices of the 25-s delayed reward in a T-maze[2]. Vofopitant (GR205171, 30 mg/kg, i.p.) increases the extracellular 5-HT levels in the frontal cortex of paroxetine-treated wild-type mice, rather than in wild-type mice and paroxetine-treated NK1 receptor knockout mice[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Tachykinin NK_1 receptor binding assays are carried out in an assay volume of 200 μL, consisting of 50 μL of wash buffer (containing HEPES (50 mM) and $MnC1_2$ (3 mM), pH 7.4) or test compound (Vofopitant), 100 μL membrane suspension (3-5 μg of protein) in HEPES assay buffer (composition as above, but containing bacitracin, 80 μg/mL], leupeptin, 8 μg/mL], phosphoramidon, 2 μM and bovine serum albumin, 0.04%) and 50 μL of [^{3}H]substance P (0.7-1.0 nM final concentration). The incubation is carried out at room temperature for 40 min. Non-specific binding is defined by the addition of CP-99,994 (1 μM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Effect of NK_1 receptor antagonists administered i.p. on cortical [5-HT]ext of wild-type mice. Following collection of four baseline dialysate samples, freely moving wild-type mice are administered with either the vehicle or various NK1 receptor

	antagonists, Vofopitant (30 mg/kg; i.p.) or L733060 (40 mg/kg; i.p.). Dialysate samples are collected for a 0-120 min post-treatment period[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Gardner CJ, et al. GR205171: a novel antagonist with high affinity for the tachykinin NK1 receptor, and potent broad-spectrum anti-emetic activity. Regul Pept. 1996 Aug 27;65(1):45-53.

[2]. Loiseau F, et al. Antidepressant-like effects of agomelatine, melatonin and the NK1 receptor antagonist GR205171 in impulsive-related behaviour in rats. Psychopharmacology (Berl). 2005 Oct;182(1):24-32. Epub 2005 Sep 29.

[3]. Guiard BP, et al. Blockade of substance P (neurokinin 1) receptors enhances extracellular serotonin when combined with a selective serotonin reuptake inhibitor: an in vivo microdialysis study in mice. J Neurochem. 2004 Apr;89(1):54-63.

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