Velusetrag

Cat. No.: HY-10457

CAS No.: 866933-46-2

Molecular Formula: $C_{25}H_{36}N_4O_5S$

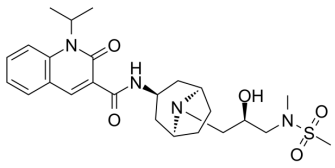
Molecular Weight: 504.64

Target: 5-HT 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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (198.16 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9816 mL	9.9081 mL	19.8161 mL
	5 mM	0.3963 mL	1.9816 mL	3.9632 mL
	10 mM	0.1982 mL	0.9908 mL	1.9816 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5.75 mg/mL (11.39 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5.48 mg/mL (10.86 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Velusetrag (TD-5108) is an orally active, potent and selective agonist of serotonin 5-HT_4 receptor (5-HT4R), with a pK_i of 7.7. Velusetrag exhibits no affinity (K_i>10 μM) for 5-HT_{2A} and 5-HT_{2B} receptors. Velusetrag can be used for the research of gastrointestinal diseases and Parkinson's disease[1][2][3][4][5].

IC_{50} & Target

5-HT_4 Receptor
7.7 (pKi)

In Vitro

Velusetrag (10 pM-100 μM) concentration-dependently increases the cAMP in HEK-293 cells stably transfected with the h5-HT4(c) receptor, with a pEC_{50} of 8.3[1].
Velusetrag (100 pM-1 μM) produces concentration-dependent contraction of the guinea pig colonic longitudinal

muscle/myenteric plexus (LMMP), with a pEC_{50} of 7.9[1].
Velusetrag (0.001-10 μM) produces a concentration-dependent relaxation of the carbachol (3 μM)-precontracted rat esophagus, with a pEC_{50} of 7.9[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Velusetrag (3 mg/kg; a single i.p.) significantly improves the facilitation of contextual fear extinction in PD mice[3].
Velusetrag (3 mg/kg; a single i.p.) increases hippocampal cAMP levels in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated mice[3].
Velusetrag (0.003-3 mg/kg; a single s.c.) increases colonic transit in a dose-dependent manner and reduces the time taken for excretion of the dye in guinea pigs[2].
Velusetrag (0.003-1 mg/kg; a single i.v.) dose-dependently increases inter-crystal distance, consistent with relaxation of the oesophagus in rats[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57BL/6 mice (7-8 weeks old) were injected with MPTP[3]
Dosage:	3 mg/kg
Administration:	A single i.p.
Result:	Improved facilitation of contextual fear extinction. Did not improve the impaired rotarod performance in PD mice.

REFERENCES

[1]. Smith JAM, et, al. The in vitro pharmacological profile of TD-5108, a selective 5-HT(4) receptor agonist with high intrinsic activity. Naunyn Schmiedebergs Arch Pharmacol. 2008 Jul;378(1):125-37.

[2]. Beattie DT, et, al. The in vivo gastrointestinal activity of TD-5108, a selective 5-HT(4) receptor agonist with high intrinsic activity. Naunyn Schmiedebergs Arch Pharmacol. 2008 Jul;378(1):139-47.

[3]. Ishii T, et, al. Serotonin 5-HT 4 Receptor Agonists Improve Facilitation of Contextual Fear Extinction in an MPTP-Induced Mouse Model of Parkinson's Disease. Int J Mol Sci. 2019 Oct 26;20(21):5340.

[4]. Kuo B, et al. Velusetrag accelerates gastric emptying in subjects with gastroparesis: a multicentre, double-blind, randomised, placebo-controlled, phase 2 study. Aliment Pharmacol Ther. 2021;53(10):1090-1097.

[5]. Goldberg M, et al. Clinical trial: the efficacy and tolerability of velusetrag, a selective 5-HT4 agonist with high intrinsic activity, in chronic idiopathic constipation - a 4-week, randomized, double-blind, placebo-controlled, dose-response study. Alime

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