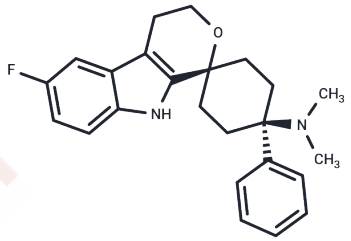
Data Sheet (Cat.No.T5167)

TargetMol

Cebranopadol

Chemical Properties



CAS No. : 863513-91-1

Formula: C24H27FN2O

Molecular Weight: 378.48

Storage: Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Cebranopadol (GRT6005) is an analgesic NOP and opioid receptor agonist with Kis of 0.9 nM, 0.7 nM, 2.6 nM, 18 nM for human NOP, μ-opioid (MOP), κ-opioid (KOP) and δ-opioid (DOP) receptor, respectively.
Targets(IC50)	Opioid Receptor
In vitro	Cebranopadol showed full agonistic efficacy at the human MOP and DOP receptors, almost full efficacy at the human NOP receptor, and partial efficacy at the human KOP receptor. In a functional [35S]GTPgS binding assay with membranes expressing the human 5-HT5A receptor, cebranopadol did not show agonistic or signirficant antagonistic effects at concentrations up to 10.0 μM [1].
In vivo	Cebranopadol displays potent and efficacious antinociceptive and antihypersensitive effects in various rat models of acute and chronic pain, with ED50 values ranging from 0.5-5.6 μg/kg intravenously and 25.1 μg/kg orally. Its action lasts up to 7 hours intravenously (12 μg/kg) and over 9 hours orally (55 μg/kg) [1]. In streptozotocin (STZ)-treated rats, cebranopadol (i.pl.) reduced mechanical hypersensitivity in the ipsilateral paw without affecting the contralateral paw. In CCI rats, cebranopadol (i.pl.) exhibited antiallodynic activity in the ipsilateral paw and, following administration to the contralateral paw, demonstrated ipsilateral antiallodynic activity with reduced potency and delayed onset. In diabetic mice, cebranopadol (i.th. and i.c.v.) effectively decreased heat hyperalgesia with similar potency for both routes [2]. In NOP(-/-) mice, morphine induced withdrawal symptoms comparable to those in NOP(+/+) animals, while cebranopadol elicited a more pronounced withdrawal syndrome in NOP(-/-) than in NOP(+/+) mice [3].
Kinase Assay	Rat MOP, KOP, and NOP receptor binding assays were run using membrane suspensions from rat brain without the cerebellum for MOP receptors; without the pons, medulla oblongata, and cerebellum for NOP receptors; and without the pons, medulla oblongata, cerebellum, and cortex for KOP receptors and the following tritium-labeled radioligands: [3H]DAMGO in the MOP receptor assay, [3H]nociceptin in the NOP receptor assay, and [3H]Ci-977 in the KOP receptor assay. The assay buffer used for the binding studies was 50 mM Tris-HCl (pH 7.4) supplemented with 0.05% sodium azide. The final assay volume of 250 μl/well included 2 nM [3H]DAMGO, 1 nM [3H]nociceptin, or 1 nM [3H]Ci-977 as a ligand in the MOP, NOP, or KOP receptor assays, respectively, and cebranopadol in dilution series. Cebranopadol was diluted with 25% DMSO in water to

Kinase Assay	yield a final 0.5% DMSO concentration, which also served as a respective vehicle control. The assays were started by the addition of the membrane suspensions and, after short mixing, the assays were run for 90 minutes at room temperature. All incubations were run in triplicate and terminated by rapid filtration under mild vacuum and two washes of 5 ml of buffer using FP-100 Whatman GF/B filter mats. The radioactivity of the samples was counted after a stabilization and extraction period of at least 15 hours by use of the scintillation fluid Ready Protein; the complete competition curves for cebranopadol were recorded [1].
Animal Research	The pharmacokinetic properties of cebranopadol in rats were investigated after a single intravenous dose of 160 µg/kg cebranopadol. The intravenous dose was administered as a bolus in a volume of 2 ml/kg with a catheter in the vena femoralis. Blood samples (200 µl/sample) were withdrawn via an implanted arterial catheter (arteria carotis) by an automated blood sampling system at the following sampling times: 0 (predose), 5, 15, 30, 60, 180, 360, 720, and 1440 minutes after administration. Blood samples were centrifuged, and plasma was separated. Plasma concentrations of cebranopadol were determined using a validated liquid chromatography-tandem mass spectrometry method. The lower limit of quantification for cebranopadol in this method was 0.05 ng/ml using a sample volume of 50 µl of plasma [1].

Solubility Information

Solubility	DMSO: 5 mg/mL (13.21 mM),Sonication is recommended. H2O: Insoluble, (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6421 mL	13.2107 mL	26.4215 mL
5 mM	0.5284 mL	2.6421 mL	5.2843 mL
10 mM	0.2642 mL	1.3211 mL	2.6421 mL
50 mM	0.0528 mL	0.2642 mL	0.5284 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Linz K, et al. Cebranopadol: a novel potent analgesic nociceptin/orphanin FQ peptide and opioid receptor agonist. J Pharmacol Exp Ther. 2014 Jun;349(3):535-48.

Tzschentke TM, et al. Antihyperalgesic, Antiallodynic, and Antinociceptive Effects of Cebranopadol, a Novel Potent Nociceptin/Orphanin FQ and Opioid Receptor Agonist, after Peripheral and Central Administration in Rodent Models of Neuropathic Pain. Pain Pract. 2017 Nov;17(8):1032-1041.

Ruzza C, et al. NOP agonist action of cebranopadol counteracts its liability to promote physical dependence. Peptides. 2019 Feb;112:101-105.

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