

Product Data Sheet

Product Name: RHC 80267

Cat. No.: GC12411

Chemical Properties

Cas. No. 83654-05-1

Chemical Name cyclohexanone O-((E)-((6-((E)-(((cyclohexylideneamino)oxy)(hydroxy)methylene)amino)hexyl)imino)(hydroxy)methyl oxime

SMILES O/C(O/N=C1CCCCC/1)=N\CCCCC/N=C(O/N=C2CCCCC/2)\O

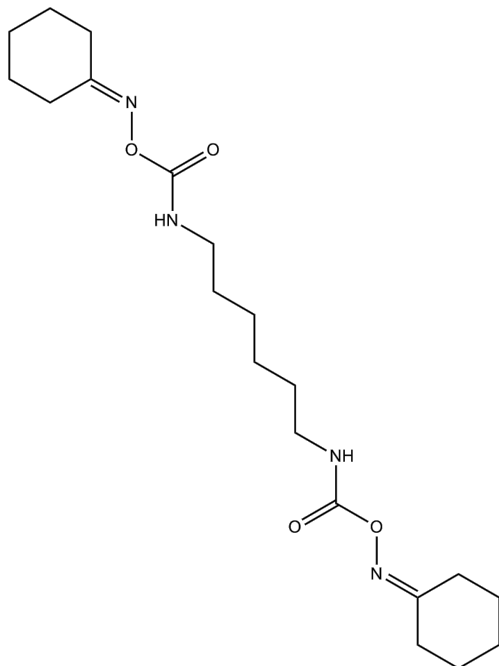
Formula $C_{20}H_{34}N_4O_4$ M.Wt 394.51

Solubility DMF: 15 mg/ml, DMF:PBS(pH 7.2) (1:1): 0.5 mg/ml, DMSO: 5 mg/ml, Ethanol: 5 mg/ml
Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Caution: Product has not been fully validated for medical applications. For research use only.

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Protocol

Cell experiment [1]:

Cell lines GH3 pituitary cells (rat anterior pituitary tumor cell line)

Preparation Method GH3 cells were maintained in Ham's F-10 medium supplemented with 10% fetal bovine serum at 37°C, 5% CO₂. GH3 cells were treated with RHC 80267 at concentrations ranging from 10-100µM for 1-4 hours.

Reaction Conditions 10-100µM; 1-4h

Applications RHC 80267 significantly inhibited basal prolactin secretion in a dose-dependent manner, with higher concentrations (50-100µM) maintaining inhibition for up to 4 hours. RHC 80267 (10µM) completely blocked TRH-induced and phospholipase C-induced prolactin secretion but did not affect PMA-stimulated secretion. RHC 80267 (10-50µM) concentration-dependently inhibited potassium-stimulated ⁴⁵calcium influx, suggesting blockade of voltage-dependent calcium channels as an alternative mechanism for its inhibitory actions on prolactin secretion.

Animal experiment [2]:

Animal models C57BL/6 mice

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Preparation Method Mice were administered Pilocarpine (100mg/kg; i.p.) to induce status epilepticus (SE), followed by Diazepam (10mg/kg; i.p.) after 70 minutes to terminate seizures. RHC 80267 (1.3µmol/animal) was administered intracerebroventricularly (i.c.v.) immediately after SE termination and once daily for the next 7 days. Control groups received vehicle injections. Mice were monitored for spontaneous recurrent seizures (SRS) from weeks 3-6 post-SE and underwent behavioral tests (open field, elevated plus maze, tail suspension, Morris water maze) during weeks 7-10.

Dosage form 1.3µmol/animal; i.c.v.; Once daily for 7 days.

Applications RHC 80267 treatment significantly reduced the percentage of mice experiencing SRS and decreased seizure duration. RHC 80267 attenuated depression- and anxiety-like behaviors, improved spatial learning and memory in the Morris water maze, and inhibited hippocampal neuronal loss in the CA1 region during the chronic epileptic period.

References:

- [1] Camoratto AM, Grandison L. Effects of RHC 80267, a diglyceride lipase inhibitor, on prolactin secretion and calcium uptake in GH3 pituitary cells. Life Sci. 1987 Jan 19;40(3):275-81.
- [2] Ma L, Wang L, Yang F, et al. Disease-modifying effects of RHC80267 and JZL184 in a pilocarpine mouse model of temporal lobe epilepsy. CNS Neurosci Ther. 2014 Oct;20(10):905-15.

Background

RHC 80267 is a potent and selective diacylglycerol lipase (DAGL) inhibitor. RHC 80267 can also inhibit cholinesterase activity ($IC_{50}=4\mu M$), suppress cyclooxygenase (COX) activity, and inhibit phosphatidylcholine hydrolysis^[1-2]. RHC 80267 functions by inhibiting diacylglycerol lipase, and RHC 80267 can be used in research related to the nervous system, cardiovascular system, and metabolic diseases^[3-4].

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In vitro, RHC 80267 (100 μ M) was used to pretreat rat cortical astrocytes for 2-6 hours, followed by culture under combined glucose-oxygen deprivation conditions. RHC 80267 significantly inhibited ischemia-induced arachidonic acid metabolite release but exacerbated cellular damage^[5]. RHC 80267 (10–100 μ M) was used to treat GH3 pituitary cells for 1-4 hours. RHC 80267 inhibited prolactin secretion from the cells and blocked potassium-stimulated calcium influx^[6].

In vivo, in a mouse model of temporal lobe epilepsy induced by pilocarpine, RHC 80267 (1.3 μ mol/animal; for 7 consecutive days) was administered via intracerebroventricular injection. RHC 80267 significantly reduced the incidence and duration of spontaneous recurrent seizures during the chronic phase, improved anxiety- and depression-like behaviors, enhanced spatial learning and memory capacity, and inhibited neuronal loss in the hippocampal CA1 region^[7].

References:

- [1] Chuang M, Severson DL. Inhibition of diacylglycerol metabolism in isolated cardiac myocytes by U-57 908 (RHC 80267), a diacylglycerol lipase inhibitor. J Mol Cell Cardiol. 1990 Sep;22(9):1009-16.
- [2] Sutherland CA, Amin D. Relative activities of rat and dog platelet phospholipase A2 and diglyceride lipase. Selective inhibition of diglyceride lipase by RHC 80267. J Biol Chem. 1982 Dec 10;257(23):14006-10.
- [3] Ghisdal P, Vandenberg G, Hamaide MC, et al. The diacylglycerol lipase inhibitor RHC-80267 potentiates the relaxation to acetylcholine in rat mesenteric artery by anti-cholinesterase action. Eur J Pharmacol. 2005 Jul 4;517(1-2):97-102.
- [4] Oglesby TD, Gorman RR. The inhibition of arachidonic acid metabolism in human platelets by RHC 80267, a diacylglycerol lipase inhibitor. Biochim Biophys Acta. 1984 Apr 18;793(2):269-77.
- [5] Haun SE, Trapp VL, Clotz MA, et al. Nordihydroguaiaretic acid and RHC 80267 potentiate astroglial injury during combined glucose-oxygen deprivation. Mol Chem Neuropathol. 1995 May;25(1):35-49.
- [6] Camoratto AM, Grandison L. Effects of RHC 80267, a diglyceride lipase inhibitor, on prolactin secretion and calcium uptake in GH3 pituitary cells. Life Sci. 1987 Jan 19;40(3):275-81.
- [7] Ma L, Wang L, Yang F, et al. Disease-modifying effects of RHC80267 and JZL184 in a pilocarpine mouse model of temporal lobe epilepsy. CNS Neurosci Ther. 2014 Oct;20(10):905-15.

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