For Research Use Only

ABX-1431

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Catalog Number: CM04959

产品信息

Catalog Number:
CM04959

CAS号:
1446817-84-0

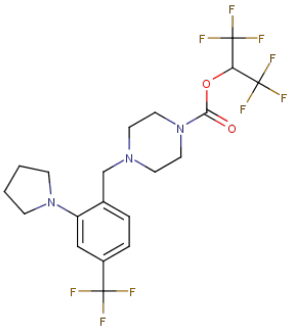
分子式:
$C_{20}H_{22}F_9N_3O_2$

主要靶点:
Lipase

主要通路:
代谢

分子量:
507.39

溶解度:
Ethanol:10 mg/mL (19.71 mM),DMSO:100 mg/mL (197.08 mM),H2O:Insoluble



靶点活性

mMGLL:27 nM|hMGLL:14 nM

体外活性

ABX-1431 was a potent human MGLL inhibitor (average IC50 = 0.014 μM) with >100-fold selectivity against ABHD6 and >200-fold selectivity against PLA2G7. Treatment of intact human PC3 cells with ABX-1431 following a 30-minute inhibitor incubation time caused concentration-dependent inhibition of MGLL activity with an IC50 value of 0.0022 μM, which is ~6-fold more potent than that observed in vitro. In the cell-based assay, >100-fold selectivity for MGLL over ABHD6 (IC50 = 0.253 μM) and PLA2G7 (IC50 = 494 μM) was maintained.

体内活性

In vivo, ABX-1431 inhibits MGLL activity in rodent brain (ED50 = 0.5-1.4 mg/kg), increases brain 2-AG concentrations, and suppresses pain behavior in the rat formalin pain model.

动物实验

All animals were 6?8 weeks old at the time of study and weighed between 197-217 g. Animals (n = 3 per dosing route) were dosed with ABX-1431 at 1 mg/kg iv (in 70% polyethylene glycol (PEG) 400 in hydroxypropyl-?-cylcodextran (HPBCD) in saline) or 5 mg/kg po (in 70% PEG 400 in 0.5% carboxymethylcellulose (CMC, w/v) in saline). Animals were fasted overnight, and food withheld until 4 h post dose. Approximately 100 μL of blood were collected via a jugular vein catheter at 0.033, 0.083, 0.25, 0.5, 1, 2, 4, 6, 8, and 24 h after intravenous and 0.25, 0.5, 1, 2, 4, 6, 8, and 24 h after oral administration. All blood samples were collected into tubes containing 400 μL acetonitrile to immediately inactivate blood esterase activity and frozen at ?80 °C. Samples were thawed and centrifuged (14,000 rpm for 5 min at 4 °C) and the supernatant transferred for LCMS analysis.

细胞实验

Human prostate cancer PC3 cells were grown in F-12K medium supplemented with 10% fetal bovine serum at 37°C with 5% CO2 to ~80% confluency in 100 mm dishes. ABX-1431 was added to cells to give final concentration of 0.1–10 μM compound in serum free media. Cells were incubated with compound for 30 min at 37°C with 5% CO2. Cells were washed, harvested, and lysed by probe sonication. Cell lysates (2mg/mL) were treated with JW912 (1 μM) and analyzed by SDS-PAGE and in-gel fluorescence scanning.

描述

ABX-1431 is a selective and orally available CNS-penetrant monoacylglycerol lipase (MAGL/MGLL) inhibitor (IC50: 14 nM).

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years