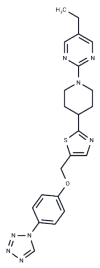
Data Sheet (Cat.No.T1793)

TargetMol

MBX-2982

Chemical Properties



CAS No. : 1037792-44-1

Formula: C22H24N8OS

Molecular Weight: 448.54

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	MBX-2982 is a selective, orally available GPR119 agonist used in the treatment of diabetes.
Targets(IC50)	GPCR
In vitro	In cells that underwent chronic incubation and subsequent washout with MBX-2982 (1 μM), a significant rise in cAMP levels was observed, as measured by IBMX inclusion, when compared to control cells, indicating enhanced accumulation despite thorough washing to eliminate any excess agonist (P<0.01; ANOVA; n=3-6). Similarly, AR-231,453 elicited prolonged responses within a comparable concentration range to acute exposure, showing a modest increase in potency (1.82-fold difference), with pEC50 values of 8.67±0.11 for sustained exposure and 8.93±0.17 for acute. Furthermore, MBX-2982 displayed a substantial yet smaller alteration in concentration response curves during sustained versus acute exposure (57.54-fold difference), with pEC50 values of 7.03±0.13 for sustained and 8.79±0.12 for acute treatment[1].
In vivo	To determine the physiological relevance of findings in GLUTag and primary intestinal cells, C57BL/6 mice were administered 10 mg/kg of the GPR119 agonist MBX-2982, without co-administration of a DPP-IV inhibitor, to assess the direct effects of GPR119 activation. However, a DPP-IV inhibitor was utilized to maintain active GLP-1 levels in blood samples. Results showed elevated plasma GLP-1 levels in mice treated with MBX-2982, even in the absence of a glucose load, demonstrating that GPR119-induced GLP-1 secretion does not require glucose (2).
Kinase Assay	HEK-GPR119 cells are transfected with GloSensor 22F plasmid and used for dynamic cAMP measurements 24-30 h later. Cell suspensions are made by dislodging the cells using PBS wash and Accutase treatment followed by resuspension in culture media. Cells are then washed twice by pelleting through centrifugation (300 g, 5 min) and resuspension in assay buffer (Hank's Balanced Salt Solution supplemented with 20 mM HEPES and 0.01% fatty acid free BSA, pH 7.4). Cells are then counted and diluted to 600,000 cells/mL in buffer, before GloSensor cAMP reagent is added (2% v/v) and equilibrated with the cells for 2 h at 20°C with periodic mixing. 50 μl/well of cells are added to white-bottomed 384 well plates (30,000 cells/well) in triplicate and baseline luminescence is measuring using an Envision plate-reader. 5 μL of MBX-2982 (serially diluted in DMSO and then diluted 1:100 in assay buffer to obtain ×10 concentrated solution) is manually added to the assay wells to achieve the stated final concentration. Plates are incubated at 20°C with luminescence read at regular intervals to detect

	dynamic cAMP changes over time within the same wells. cAMP responses at each time-point are expressed as fold over control (vehicle-treated cells)[1].
Cell Research	MBX-2982 is serially diluted in DMSO and then diluted 1:100 in assay buffer to obtain ×10 concentrated solutionis[1]. HEK-GPR119 cells are grown to confluency in flasks, and cell suspensions are made by dislodging cells using PBS wash and accutase treatment followed by resuspension in culture media. Cells are then washed twice by pelleting through centrifugation (227 g, 7 min, 20°C) and resuspension in warm assay buffer (Hank's Balanced Salt Solution supplemented with 20 mM HEPES and 0.01% fatty acid free BSA, pH 7.4), with a 5 min incubation at 37°C after the second wash. Cells are then counted and diluted to 200,000 cells/mL in warm assay buffer[1].

Solubility Information

Solubility	DMSO: 50 mg/mL (111.47 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2295 mL	11.1473 mL	22.2946 mL
5 mM	0.4459 mL	2.2295 mL	4.4589 mL
10 mM	0.2229 mL	1.1147 mL	2.2295 mL
50 mM	0.0446 mL	0.2229 mL	0.4459 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.

Reference

Hothersall JD, et al. Sustained wash-resistant receptor activation responses of GPR119 agonists. Eur J Pharmacol. 2015 Sep 5;762:430-42.

Lan H, et al. Agonists at GPR119 mediate secretion of GLP-1 from mouse enteroendocrine cells through glucose-independent pathways. Br J Pharmacol. 2012 Apr;165(8):2799-807.