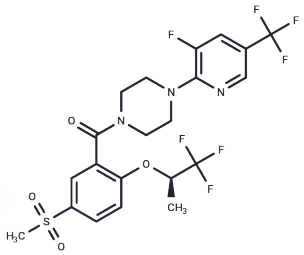
Data Sheet (Cat.No.T10552)

TargetMol

Bitopertin (R enantiomer)

Chemical Properties



CAS No. : 845614-12-2

Formula: C21H20F7N3O4S

Molecular Weight: 543.46

Storage: 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	Bitopertin R enantiomer (RG1678 R enantiomer) is the R-enantiomer of Bitopertin, a noncompetitive glycine reuptake inhibitor that inhibits glycine uptake at human GlyT1 (IC50: 25 nM).
Targets(IC50)	GlyT
In vitro	Bitopertin (RG1678) competitively blocks [3H]ORG24598 binding sites at human GlyT1b in membranes from Chinese hamster ovary cells. In cells stably expressing hGlyT1b and mGlyT1b, Bitopertin potently inhibits [3H]glycine uptake (IC50s: 25 nM and 22 nM). Conversely, Bitopertin has no effect on hGlyT2-mediated glycine uptake up to 30 μM concentration. Bitopertin has a high affinity for the recombinant hGlyT1b transporter. Under equilibrium conditions (1 h at room temperature), Bitopertin displaces [3H] ORG24598 binding (Ki: 8.1 nM). In hippocampal CA1 pyramidal cells, Bitopertin enhances NMDA-dependent long-term potentiation at 100 nM but not at 300 nM [1]. Bitopertin has an excellent selectivity profile against the GlyT2 isoform (IC50>30 μM) and toward a panel of 86 targets including transmembrane and soluble receptors, enzymes, ion channels, and monoamine transporters (<41% inhibition at 10 μM is measured for all targets) [2].
In vivo	Bitopertin dose-dependently increases cerebrospinal fluid (CSF) and striatal glycine levels measured by microdialysis in rats, attenuates hyperlocomotion induced by D-amphetamine or NMDA receptor glycine site antagonist L-687,414 in mice, and prevents hyper-response to D-amphetamine in rats chronically treated with phencyclidine. Vehicle administration has no effect on extracellular striatal glycine levels. Oral administration of Bitopertin (1-30 mg/kg) dose-dependently increases extracellular glycine levels, with a 30 mg/kg dose resulting in a 2.5-fold increase. Similar dose-dependent increases in CSF glycine concentration are observed in rats treated with Bitopertin (1-10 mg/kg) compared to vehicle-treated animals, 3 hours post-administration [1]. In vivo pharmacokinetic studies reveal that Bitopertin has low plasma clearance, intermediate volume of distribution, good oral bioavailability (78% in rats, 56% in monkeys), favorable terminal half-life (5.8 h in rats, 6.4 h in monkeys), high plasma protein binding (97% in preclinical species, 98% in humans), and better CNS penetration in rats (brain/plasma=0.7) than in mice (brain/plasma=0.5) [2].

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8401 mL	9.2003 mL	18.4006 mL
5 mM	0.368 mL	1.8401 mL	3.6801 mL
10 mM	0.184 mL	0.920 mL	1.8401 mL
50 mM	0.0368 mL	0.184 mL	0.368 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

Alberati D, et al. Glycine reuptake inhibitor RG1678: A pharmacologic characterization of an investigational agent for the treatment of schizophrenia. Neuropharmacology. 2012 Feb;62(2):1152-61.
Pinard E, et al. Selective GlyT1 Inhibitors: Discovery of [4-(3-Fluoro-5-trifluoromethylpyridin-2-yl)piperazin-1-yl][5-methanesulfonyl-2-((S)-2,2,2-trifluoro-1-methylethoxy)phenyl]methanone (RG1678), a Promising Novel Medicine To Treat Schizophrenia. J Me
Alberati, Daniela; Moreau, Jean-Luc; Lengyel, Judith et al. Glycine reuptake inhibitor RG1678: A pharmacologic characterization of an investigational agent for the treatment of schizophrenia. Neuropharmacology (2012), 62(2), 1152-1161.
Hofmann C, Banken L, Hahn M et al. Evaluation of the Effects of Bitopertin (RG1678) on Cardiac Repolarization: A Thorough Corrected QT Study in Healthy Male Volunteers. Clin Ther. 2012 Oct;34(10):2061-71.
Martin-Facklam M, Pizzagalli F, Zhou Y et al. Glycine Transporter Type 1 Occupancy by Bitopertin: a Positron Emission Tomography Study in Healthy Volunteers. Neuropsychopharmacology. 2012 Nov 7. doi: 10.1038/npp.2012.212. [Epub ahead of print]