Web: www.taiclone.com
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Bitopertin (R enantiomer)

Catalog No: tcsc1261

Available Sizes

Size: 1mg

Specifications

CAS No:
845614-12-2

Formula:
$C_{21}H_{20}F_7N_3O_4S$

Pathway:
Neuronal Signaling;Membrane Transporter/Ion Channel

Target:
GlyT;GlyT

Purity / Grade:
>98%

Solubility:
10 mM in DMSO

Alternative Names:
RG1678 (R enantiomer);RO4917838 (R enantiomer)

Observed Molecular Weight:
543.46

Product Description

Bitopertin is a potent, noncompetitive **glycine reuptake** inhibitor, inhibits glycine uptake at human **GlyT1** with a concentration exhibiting **IC50** of 25 nM.

IC50 & Target: IC50: 25 nM (GlyT1)[1]

In Vitro:

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Bitopertin (RG1678) competitively blocks [^{3}H]ORG24598 binding sites at human GlyT1b in membranes from Chinese hamster ovary cells. Bitopertin potently inhibits [^{3}H]glycine uptake in cells stably expressing hGlyT1b and mGlyT1b, with IC_{50} values of 25±2 nM and 22±5 nM, respectively (n=6). Conversely, Bitopertin has no effect on hGlyT2-mediated glycine uptake up to 30 μM concentration. Bitopertin has high affinity for the recombinant hGlyT1b transporter. Under equilibrium conditions (1 h at room temperature), Bitopertin displaces [^{3}H]ORG24598 binding with a K_i of 8.1 nM. In hippocampal CA1 pyramidal cells, Bitopertin enhances NMDA-dependent long-term potentiation at 100 nM but not at 300 nM[1]. Additional profiling revealed that Bitopertin (RG1678) has an excellent selectivity profile against the GlyT2 isoform (IC_{50}>30 μM) and toward a panel of 86 targets including transmembrane and soluble receptors, enzymes, ion channels, and monoamine transporters ([2].

In Vivo: Bitopertin (RG1678) dose-dependently increases cerebrospinal fluid and striatal levels of glycine measured bymicrodialysis in rats. Additionally Bitopertin attenuates hyperlocomotion induced by the psychostimulant D-amphetamine or the NMDA receptor glycine site antagonist L-687,414 in mice. Bitopertin also prevents the hyper-response to D-amphetamine challenge in rats treated chronically with phencyclidine, an NMDA receptor open-channel blocker. Administration of vehicle has no effect on extracellular levels of striatal glycine, which remained constant throughout the experiment. In contrast, p.o. administration of Bitopertin (1-30 mg/kg) produced a dose-dependent increase in extracellular glycine levels. Bitopertin 30 mg/kg produces glycine levels 2.5 times higher than pretreatment levels. A similar dose-dependent increase in glycine concentration is observed in the CSF of rats treated p.o. with Bitopertin (1-10 mg/kg) compared with vehicle-treated animals, 3 h after drug administration. Interestingly, the level of CSF glycine increase 3 h after Bitopertin dosing is very similar to the increase in the microdialysis experiment at the same time point[1]. In vivo pharmacokinetic studies in rat and monkey reveals that Bitopertin (RG1678) has, in both species, a low plasma clearance, an intermediate volume of distribution, a good oral bioavailability (78% for rat, 56% for monkey), and a favorable terminal half-life (5.8 h for rat, 6.4 h for monkey). The plasma protein binding is high in the two preclinical species (97%) and in human (98%). The CNS penetration of Bitopertin in rat (brain/plasma=0.7) is better than that in mouse (brain/plasma=0.5)[2].