CYM5442 hydrochloride

Cat. No.: HY-10968A

CAS No.: 1783987-80-3

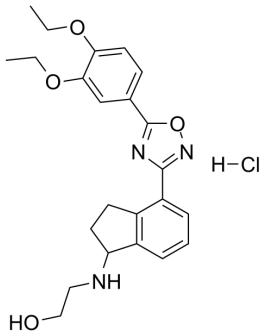
Molecular Formula: $C_{23}H_{28}ClN_3O_4$

Molecular Weight: 445.94

Target: LPL Receptor

Pathway: GPCR/G Protein

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CYM5442 hydrochloride is a potent, highly-selective and orally active sphingosine 1-phosphate (S1P1) receptor agonist with an EC_{50} of 1.35 nM. CYM5442 hydrochloride is inactive against S1P2, S1P3, S1P4, and S1P5. CYM5442 hydrochloride activates S1P1-dependent p42/p44-MAPK phosphorylation. CYM5442 exerts retinal neuroprotection. CYM5442 hydrochloride can easily penetrate the central nervous system (CNS)[1][2].

IC_{50} & Target

EC50: 1.35 nM (Sphingosine 1-phosphate (S1P1) receptor)[1]

In Vitro

CYM5442 (0.5 μM; 0-60 minutes; HEK293 cells) treatment stimulates S1P1 phosphorylation in a time-dependent manner in P32-orthophosphate labeled cells[1].

CYM5442 activates S1P1-dependent p42/p44-MAPK phosphorylation in CHO-K1 cells transfected with S1P1 with an EC_{50} of 46 nM. The R120 for alanine (R120A) mutant is still able to maintain p42/p44-MAPK activity when incubated with CYM5442 (EC_{50} of 67 nM). Activation of p42/p44-MAPK by CYM-5442 in E121A S1P1 cells is concentration dependent, with a mean EC_{50} value of 134 nM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	HEK293 cells stably expressing S1P1 fused to GFP on the carboxy-terminus
Concentration:	0.5 μM
Incubation Time:	0 minutes, 2 minutes, 5 minutes, 10 minutes, 30 minutes, 60 minutes
Result:	Stimulated S1P1 phosphorylation in a time-dependent manner.

In Vivo

CYM5442 (1 mg/kg; intraperitoneal injection; daily; for 5 days; adult male albino Wistar rats) treatment shows preserved visual function of visual evoked potentials (VEP). Retinal nerve fiber layer (RNFL) is significantly thicker in the CYM treated-animals compared to the vehicle[2].

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Animal Model:	Adult male albino Wistar rats (8-10 weeks old; 180-230 g) infected ocular endothelin-1 (ET-1)[2]

Dosage:	1 mg/kg
Administration:	Intraperitoneal injection; daily; for 5 days
Result:	Visual evoked potentials (VEP) showed preserved visual function. Showed significantly higher retinal ganglion cells (RGCs) numbers.

REFERENCES

[1]. Gonzalez-Cabrera PJ, et al. Full pharmacological efficacy of a novel S1P1 agonist that does not require S1P-like headgroup interactions. Mol Pharmacol. 2008 Nov;74(5):1308-18.

[2]. Blanco R, et al. The S1P1 receptor-selective agonist CYM-5442 protects retinal ganglion cells in endothelin-1 induced retinal ganglion cell loss. Exp Eye Res. 2017 Nov;164:37-45.

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