Lesogaberan hydrochloride

Cat. No.: HY-10061B

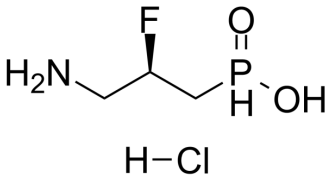
Molecular Formula: $C_3H_{10}ClFNO_2P$

Molecular Weight: 177.54

Target: GABA Receptor

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: 4°C, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 240 mg/mL (1351.81 mM; Need ultrasonic)
H_2O : 100 mg/mL (563.25 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	5.6325 mL	28.1627 mL	56.3253 mL
5 mM	1.1265 mL	5.6325 mL	11.2651 mL
10 mM	0.5633 mL	2.8163 mL	5.6325 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (563.25 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 6 mg/mL (33.80 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 6 mg/mL (33.80 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 6 mg/mL (33.80 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Lesogaberan (AZD-3355) hydrochloride is a potent and selective $GABA_B$ receptor agonist with an EC_{50} of 8.6 nM for human recombinant $GABA_B$ receptor. The affinity (K_is) of Lesogaberan hydrochloride for rat $GABA_B$ and $GABA_A$ receptors, as measured by displacement of [^{3}H]GABA binding in brain membranes: 5.1 nM and 1.4 μM, respectively. Lesogaberan hydrochloride inhibits transient lower esophageal sphincter relaxation through a peripheral mode of action[1].

IC_{50} & Target

Ki: 5.1±1.2 nM (rat $GABA_B$), 1.4±0.3 μM (rat $GABA_A$)[1]

	EC50: 8.6±0.77 nM (human $GABA_B$ receptor)[1]
In Vitro	Lesogaberan hydrochloride (3-30 nM) enhances human islet cell proliferation in vitro[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only. Cell Proliferation Assay[2]

Cell Line:	Human islet cells
Concentration:	3, 10, and 30 nM
Incubation Time:	4 days
Result:	Had a small but nonsignificant promitotic effect at 3 nM, while treatment at higher dosages (10 and 30 nM) led to a 2-3-fold increase in proliferation relative to that of islets cultured in medium alone.

In Vivo

Lesogaberan hydrochloride potently stimulates recombinant human $GABA_B$ receptors and inhibits transient lower esophageal sphincter relaxation (TLESR) in dogs, with a biphasic dose-response curve[1].
Oral Lesogaberan (0.08 mg/mL; 48 hours) hydrochloride protects human islet β-cells from apoptosis in islet grafts in mice[2].
Lesogaberan (7 μmol/kg) hydrochloride shows high oral availability (88% in the dog and 100% in the rat) and relatively low systemic clearance in female Sprague Dawley rats[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Diabetic NOD/scid mice were implanted with human islets[2]
Dosage:	0.08 mg/mL
Administration:	48 hours
Result:	Significantly reduced the percentages of apoptotic islet cells and increased the frequency of $insulin^+$ β-cells in human islet grafts.

Animal Model:	Female Sprague Dawley rats[1]
Dosage:	7 μmol/kg (Pharmacokinetic Analysis)
Administration:	Oral
Result:	High oral availability (88% in the dog and 100% in the rat) and relatively low systemic clearance. Plasma protein binding was 1% in rat and human plasma.

REFERENCES

[1]. Lehmann A, et al. (R)-(3-amino-2-fluoropropyl) phosphinic acid (AZD3355), a novel GABAB receptor agonist, inhibits transient lower esophageal sphincter relaxation through a peripheral mode of action. J Pharmacol Exp Ther. 2009 Nov;331(2):504-12.

[2]. Tian J, et al. Repurposing Lesogaberan to Promote Human Islet Cell Survival and β-Cell Replication. J Diabetes Res. 2017;2017:6403539.

Caution: Product has not been fully validated for medical applications. For research use only.

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