Calhex 231 hydrochloride

Cat. No.: HY-103320A

CAS No.: 2387505-78-2

Molecular Formula: $C_{25}H_{28}Cl_2N_2O$

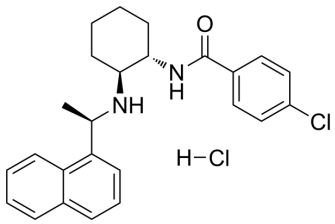
Molecular Weight: 443.41

Target: CaSR

Pathway: GPCR/G Protein

Storage: -20°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (75.17 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2552 mL	11.2762 mL	22.5525 mL
	5 mM	0.4510 mL	2.2552 mL	4.5105 mL
	10 mM	0.2255 mL	1.1276 mL	2.2552 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (5.64 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.64 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Calhex 231 hydrochloride is a potent negative allosteric modulator that blocks (IC_{50} = 0.39 μM) increases in [^{3}H]inositol phosphates elicited by activating the human wild-type CaSR transiently Ca^{2+}-sensing receptor. Calhex 231 hydrochloride can be used in the study of traumatic hemorrhagic shock (THS) and diabetic cardiomyopathy (DCM)[1].

IC_{50} & Target

CaSR[1]

IC50: 0.39 μM (Inositol phosphate)[2]

In Vitro

Calhex 231 dose-dependently inhibited the IP response induced by 10 mM Ca^{2+} with a potency in the T764A (IC_{50} = 0.28 ± 0.05 μM) and H766A (IC_{50} = 0.64 ± 0.03 μM) mutant receptors similar to that in the WT receptor[1].Calhex 231 treatment significantly downregulates the CaSR, α-SMA, Col-I/III, MMP2/9 expresses. Calhex231 alleviates high glucose-induced myocardial fibrosis in cardiac fibroblasts[2].

Calhex 231 could inhibit Itch (atrophin-1 interacting protein 4)-ubiquitin proteasome and TGF-β1/Smads pathways, and then depress the proliferation of cardiac fibroblasts, along with the reduction deposition of collagen, alleviate glucose-induced myocardial fibrosis[2].

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

Cell Proliferation Assay[1]

Cell Line:	Primary neonatal rat cardiac fibroblasts (CFs)
Concentration:	3 μM
Incubation Time:	24 hours
Result:	Significantly decreased the proliferation of cardiac fibroblasts.

Western Blot Analysis[1]

Cell Line:	Primary neonatal rat cardiac fibroblasts (CFs)
Concentration:	3 μM
Incubation Time:	48 hours
Result:	The expression of CaSR, α-SMA, Col-I/III, MMP2/9 were significantly downregulated.

In Vivo

Calhex 231 (4.07 mg/kg (10 μmol/kg); intraperitoneal injection; daily; for 12 weeks; male Wistar rats) treatment ameliorates diabetic myocardial fibrosis in type 1 diabetic model (T1D) rats[2].

Calhex-231 (Cal, 0.1-1 mg/kg) has a mitigating effect on traumatic hemorrhagic shock by improving vascular hyporesponsiveness and reducing mitochondrial dysfunction[3].

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

Animal Model:	Male Wistar rats (8 weeks old) injected with Streptozotocin[1]
Dosage:	4.07 mg/kg (10 μmol/kg)
Administration:	Intraperitoneal injection; daily; for 12 weeks
Result:	Ameliorated diabetic myocardial fibrosis in T1D rats.

Animal Model:	Four hundred and fifty Sprague-Dawley (SD) rats (half male and half female)[3].
Dosage:	0.1, 1, or 5 mg/kg.
Administration:	A continuous infusion.
Result:	In all groups, MAP, LVSP, and ±dp/dtmax decreased significantly after shock. Administration of 5 or 1 mg/kg Cal resulted in significantly increased values at 1 and 2 hr postadministration, compared to rats in the LR only group (or 0.01). Rats treated with 1 mg/kg Cal demonstrated the greatest recovery. LR infusion induced short-term and slightly increase of blood pressor in normal rats. Cal (1 mg/kg) without LR infusion did not restore the decreased MAP after shock.

CUSTOMER VALIDATION

- Front Pharmacol. 2022 Feb 23;13:816133.
- Front Pharmacol. 23 February 2022.
- Mol Nutr Food Res. 2023 Dec 31:e2200726.

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REFERENCES

[1]. Yan Lei, et al. The Calcilytic Drug Calhex-231 Ameliorates Vascular Hyporesponsiveness in Traumatic Hemorrhagic Shock by Inhibiting Oxidative Stress and miR-208a-Mediated Mitochondrial Fission. Oxid Med Cell Longev. 2020 Dec 3:2020:4132785.

[2]. Christophe Petrel, et al. Modeling and mutagenesis of the binding site of Calhex 231, a novel negative allosteric modulator of the extracellular Ca(2+)-sensing receptor. J Biol Chem. 2003 Dec 5;278(49):49487-94.

[3]. Petrel C1, et al. Modeling and mutagenesis of the binding site of Calhex 231, a novel negative allosteric modulator of the extracellular Ca(2+)-sensing receptor. J Biol Chem. 2003 Dec 5;278(49):49487-94.

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