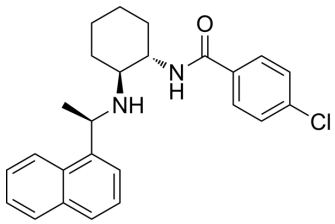
Calhex 231

Cat. No.:	HY-103320
CAS No.:	652973-93-8
Molecular Formula:	$C_{25}H_{27}ClN_2O$
Molecular Weight:	406.95
Target:	CaSR
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Calhex 231 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 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)[1]

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[2]

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

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[2]

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]. 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.

[2]. 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.

[3]. 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.

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