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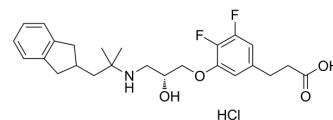
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Ronacaleret hydrochloride

Cat. No.:	HY-15104
CAS No.:	702686-96-2
Molecular Formula:	C ₂₅ H ₃₂ ClF ₂ NO ₄
Molecular Weight:	483.98
Target:	CaSR
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Ronacaleret hydrochloride (SB 751689A) is an orally active, potent, and selective calcium-sensing receptor (CaSR) antagonist that stimulates endogenous parathyroid hormone release from the parathyroid glands. Ronacaleret hydrochloride (SB 751689A) is used for the study of postmenopausal osteoporosis ^[1] .
In Vitro	Ronacaleret inhibits OATP1B1 (IC ₅₀ = 11 μM) and OATP2B1 (IC ₅₀ = 12 μM) in vitro, whereas it does not inhibit BCRP ^[3] . Ronacaleret is shown to inhibit the OATP1B1- and OATP1B3-mediated uptake of the probe substrate estradiol-glucuronide with relatively low potency (IC ₅₀ values of 11 and 60 μM, respectively) ^[3] . Ronacaleret inhibits OATP2B1-mediated rosuvastatin transport at pH 7.4 and pH 6.0, with IC ₅₀ values of 16 and 12 μM, respectively ^[3] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ronacaleret (SB 751689, 3 mg/kg/day) preserves klotho expression and renal function with the reductions in serum phosphate and albuminuria in 5/6-nephrectomized rats ^[3] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Model:	7-week-old Wistar rats ^[2] .
Dosage:	3 mg/kg/day (dissolved in 10% β-cyclodextrin solution).
Administration:	Administered by an osmotic pump that was implanted subcutaneously.
Result:	Increased renal expression of klotho in a dose-dependent manner. Decreased serum phosphate and FGF23 with the increased fractional excretion of phosphate without changes in serum calcium. Appeared to similarly protect podocytes. Reduced FGF23 and because FGF23 enhanced klotho expression.

REFERENCES

[1]. György Szabó, et al. Discovery of dihydropyrazino-benzimidazole derivatives as metabotropic glutamate receptor-2 (mGluR2) positive allosteric modulators (PAMs). Eur J Med Chem. 2020 Jan 15;186:111881.

[2]. Tsuneo Takenaka , et al. Antialbuminuric actions of calcilytics in the remnant kidney. Am J Physiol Renal Physiol. 2015 Aug 1;309(3):F216-26.

[3]. Marta Johnson, et al. Inhibition of Intestinal OATP2B1 by the Calcium Receptor Antagonist Ronacaleret Results in a Significant Drug-Drug Interaction by Causing a 2-Fold Decrease in Exposure of Rosuvastatin. Drug Metab Dispos. 2017 Jan;45(1):27-34.

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

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