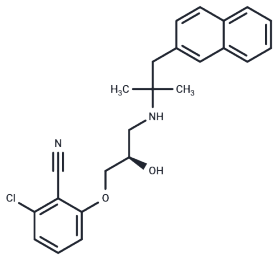
Data Sheet (Cat.No.T1730)

TargetMol

NPS-2143

Chemical Properties



CAS No. : 284035-33-2

Formula: C24H25ClN2O2

Molecular Weight: 408.92

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	NPS-2143 (SB 262470A) is a novel potent and selective antagonist of Ca(2+) receptor.
Targets(IC50)	Calcium Channel,CaSR
In vitro	NPS 2143 stimulates the secretion of parathyroid hormone (PTH) from bovine parathyroid cells with an effective concentration (EC50) of 41 nM. Moreover, NPS 2143 inhibits the suppressive effect of the calcimimetic NPS R-467 on PTH secretion from bovine parathyroid cells and the inhibition of cAMP formation stimulated by isoproterenol in the presence of extracellular Ca2+. In HEK 293 cells expressing the human Ca2+ receptor, NPS 2143 blocks the increase in cytosolic Ca2+ concentration induced by receptor activation, with an inhibitory concentration (IC50) of 43 nM. Furthermore, in HEK-293 cells transiently expressing hCaSRs, NPS 2143 significantly inhibits the umami taste perception by effectively suppressing GSH (data not shown) and γ-Glu-Val-Gly activity.
In vivo	In normotensive rats, intravenous administration of NPS 2143 (1 mg/kg) significantly increased mean arterial pressure (MAP) in the presence of the parathyroid gland. Additionally, NPS 2143 induced a rapid 4-5 fold increase in plasma parathyroid hormone (PTH) levels and an instantaneous rise in plasma calcium (Ca2+) levels.
Kinase Assay	This clonal cell line, referred to as HEK 293 4.0-7 cells, are used in a high-throughput screening format to detect agonists and allosteric activators of the Ca2+?receptor. Changes in the concentration of cytoplasmic [Ca2+]i provide a quantitative and functional assessment of Ca2+ receptor activity in these cells and the results using this assay parallel those obtained using a homologous expression system of bovine parathyroid cells. On-line continuous measurements of fluorescence in fluo-3- or fura-2-loaded HEK 293 4.0-7 cells are obtained using a custom-built spectrofluorimeter or a fluorescence imaging plate reader instrument. NPS-2143 is incubated with cells for 1 minute before increasing the concentration of extracellular Ca2+?from 1.0 mM to 1.75 mM. NPS-2143 is tested individually at a concentration of 100 μg/mL (20 μM-80 μM) and those causing more than a 40% inhibition of the control response are considered to be biologically active. To determine the potencies (IC50) of NPS-2143 with biological activity, concentration-response curves are obtained and then, as an initial assessment of selectivity, the effects of NPS-2143 on [Ca2+]i evoked by other G protein-coupled receptors are examined at a concentration several times their IC50. Wild-type HEK 293

Kinase Assay	cells (and HEK 293 4.0-7 cells) express receptors for thrombin, bradykinin, and ATP, which couple to the mobilization of intracellular Ca2+. These responses can be studied to quickly assess any nonselective action of compounds on G protein-coupled receptors. Additional assays for selectivity include HEK 293 cells engineered to express receptors most homologous in sequence and topology to the Ca2+ receptor. These include native or chimeric receptors for various metabotropic glutamate and γ-aminobutyric acid type B receptors (GABABRs).Chimeric receptors are created using partial sequences of metabotropic glutamate receptors and Ca2+?receptors, engineered to couple to activation of phospholipase C and release of intracellular Ca2+?in HEK 293 cells. NPS-2143 lacking pan-activity are then subjected to structural modifications and their potencies and selectivities monitored using these HEK 293 4.0-7 cell assays in an iterative process.

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 18.75 mg/mL (45.85 mM),, when pH is adjusted to 3 with HCl. Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4455 mL	12.2273 mL	24.4547 mL
5 mM	0.4891 mL	2.4455 mL	4.8909 mL
10 mM	0.2445 mL	1.2227 mL	2.4455 mL
50 mM	0.0489 mL	0.2445 mL	0.4891 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Nemeth EF, et al. J Pharmacol Exp Ther. 2001, 299(1), 323-331.
Rybczynska A, et al. J Endocrinol. 2006, 191(1), 189-195.
Ohsu T, et al. J Biol Chem. 2010, 285(2), 12016-1022.
Nakajima S, et al. Mol Nutr Food Res. 2012, 56(5), 753-760.