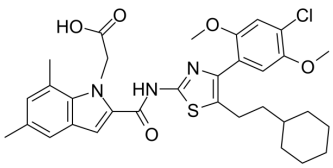
SR 146131

Cat. No.:	HY-11077
CAS No.:	221671-61-0
Molecular Formula:	$C_{32}H_{36}ClN_3O_5S$
Molecular Weight:	610.16
Target:	Cholecystokinin Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (409.73 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6389 mL	8.1946 mL	16.3891 mL
	5 mM	0.3278 mL	1.6389 mL	3.2778 mL
	10 mM	0.1639 mL	0.8195 mL	1.6389 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: 2.08 mg/mL (3.41 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (3.41 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SR 146131 is a potent, orally available, and selective nonpeptide (cholecystokinin 1) receptor agonist.

IC_{50} & Target

Cholecystokinin 1 receptor[1]

In Vitro

SR 146131 inhibits in the binding of [^{125}I]-BH-CCK-8S to CCK1sites on 3T3-hCCK1 cell membranes with an IC_{50} value of 0.56 ± 0.10 nM. At much higher concentrations, SR 146131 also inhibits the binding of radiolabeled CCK to CCK2sites in CHO-hCCK2 membranes with an IC_{50} of 162 ± 27 nM. SR 146131 is a potent CCK1 agonist on several intracellular events linked to CCK1

	receptor activation in various cell types: on $[Ca^{2+}]i$ release and IP1 formation, SR 146131 appears as a full CCK1 receptor agonist in the 3T3-hCCK1 cells, but a partial CCK1receptor agonist on MAPK activation and early gene expression in this cell line. SR 146131 also acts as a partial agonist in the two neuroblastoma cell lines[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SR 146131 completely inhibits gastric and gallbladder emptying in mice (ED_{50} of 66 and 2.7 μg/kg p.o., respectively). SR 146131 dose dependently reduces food intake in fasted rats (from 0.1 mg/kg p.o.), in nonfasted rats in which food intake has been highly stimulated by the administration of neuropeptide Y (1–36) (from 0.3 mg/kg p.o.), in fasted gerbils (from 0.1 mg/kg p.o.), and in marmosets maintained on a restricted diet (from 3 mg/kg p.o.). SR 146131 (10 mg/kg p.o.) also increases the number of Fos-positive cells in the hypothalamic paraventricular nucleus of rats. Locomotor activity of mice is reduced by orally administered SR 146131 (from 0.3 mg/kg p.o.)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	3T3-hCCK1 cells grown to subconfluence in 6-well cluster plates are washed with fresh medium. Twenty-four hours later, the cells are stimulated for 15 min with various concentrations of CCK-8S or SR 146131[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats[1] Male Sprague-Dawley rats are fasted for 18 h, and allowed access to food for only 6 h between 10 AM and 4 PM each day. Water is available ad libitum. At the end of this adaptation phase, rats are administered SR 146131 (0.03-3 mg/kg p.o.). One hour after SR 146131 administration, a weighed amount of food is introduced into the cage, and food intake is measured 1, 3, 6, and 23 h after SR 146131 administration[1]. Mice[1] SR 146131 (0.01-1 pg) is solubilized in DMSO (1 mg/mL), diluted to the required concentrations with water, and injected (in 1 μL) into one striatum in awake, hand-restrained female CD1 mice (25-30 g). After injection, the animals are placed individually in Plexiglas cages (10 × 10 × 15 cm). Turning behavior in mice is monitored[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Bignon E, et al. SR146131: a new potent, orally active, and selective nonpeptide cholecystokinin subtype 1 receptor agonist. I. In vitro studies. J Pharmacol Exp Ther. 1999 May;289(2):742-51.

[2]. Bignon E, et al. SR146131: a new potent, orally active, and selective nonpeptide cholecystokinin subtype 1 receptor agonist. II. In vivo pharmacological characterization. J Pharmacol Exp Ther. 1999 May;289(2):752-61.

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