Rolapitant

Cat. No.: HY-14751

CAS No.: 552292-08-7

Molecular Formula: $C_{25}H_{26}F_6N_2O_2$

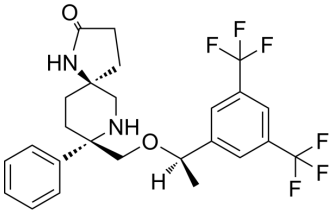
Molecular Weight: 500.48

Target: Neurokinin Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 30 mg/mL (59.94 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9981 mL	9.9904 mL	19.9808 mL
	5 mM	0.3996 mL	1.9981 mL	3.9962 mL
	10 mM	0.1998 mL	0.9990 mL	1.9981 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 (5.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Rolapitant (SCH619734) is a potent, selective, long-acting and orally active neurokinin 1 (NK1) receptor antagonist with a K_i of 0.66 nM. Rolapitant does not interact with CYP3A4. Rolapitant shows potent anti-emetic activity in a ferret emesis model [1][2].

IC_{50} & Target

human NK1 0.66 nM (Ki)	gerbil NK1 0.13 nM (Ki)	guinea pig NK1 0.72 nM (Ki)	monkey NK1 2.5 nM (Ki)
rabbit NK1 31.7 nM (Ki)	rat NK1 78.6 nM (Ki)	mouse NK1 60.4 nM (Ki)	

In Vitro

Rolapitant has high selectivity over the human NK2 and NK3 subtypes of more than 1000-fold, as well as preferential affinity for human, guinea pig, gerbil and monkey NK1 receptors over rat, mouse and rabbit[1].
Rolapitant (1-1000 nM) inhibits the GR-73632 (an NK1 receptor agonist)-induced calcium efflux with a concentration-dependent and competitive manner in CHO cells expressing the human NK1 receptor[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Rolapitant (0.03-1 mg/kg for PO, 0.3-1 mg/kg for IV; single dosage) attenuates the GR-73632-induced foot-tapping response in Mongolian Gerbils[1].
Rolapitant (0.03-1 mg/kg; PO; single dosage; observed for 72 h) blocks acute emesis induced by both apomorphine and cisplatin in ferrets[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female Mongolian Gerbils (30-60 g; anesthetized by inhalation of an oxygen:isofluorane mixture after 4 h PO or immediately after IV, then injected with 5 μl of 3 pmol solution of GR-73632 via ICV)[1]
Dosage:	0.03, 0.1, 0.3 and 1 mg/kg for PO, 0.3 and 1 mg/kg for IV
Administration:	PO or IV, single dosage
Result:	Attenuated dose-dependently the GR-73632-induced foot-tapping response when administered PO 4 h before testing, with an ID_{90} of 0.3 mg/kg, and the inhibition in foot tapping for at least 24 h. Blocked dose-dependently the foot tapping induced by GR-73632 when administered IV, with complete blockade observed at 1 mg/kg.

Animal Model:	Ferrets (treated with subcutaneous administration of 0.125 mg/kg apomorphine or intraperitoneal administration of 10 mg/kg cisplatin)[1]
Dosage:	0.03, 0.1, 0.3 and 1 mg/kg
Administration:	PO; single dosage; observed for 72 h
Result:	Blocked dose-dependently acute emesis induced by both apomorphine and cisplatin in ferrets. Produced a robust decrease in retches and vomits in ferrets that was maintained throughout the 72 h observation period.

REFERENCES

[1]. Rapoport B, et al. Study of rolapitant, a novel, long-acting, NK-1 receptor antagonist, for the prevention of chemotherapy-induced nausea and vomiting (CINV) due to highly emetogenic chemotherapy (HEC). Support Care Cancer. 2015 Nov;23(11):3281-8.

[2]. Duffy RA, et al. Rolapitant (SCH 619734): a potent, selective and orally active neurokininNK1 receptor antagonist with centrally-mediated antiemetic effects inferrets. Pharmacol Biochem Behav. 2012 Jul;102(1):95-100.

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