Rolapitant hydrochloride hydrate

Cat. No.: HY-16436

CAS No.: 914462-92-3

Molecular Formula: $C_{25}H_{29}ClF_6N_2O_3$

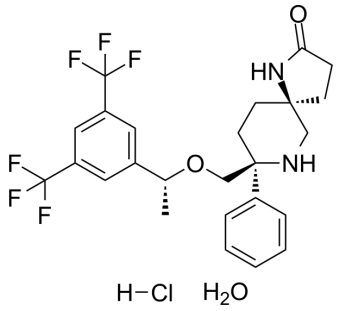
Molecular Weight: 554.95

Target: Neurokinin Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (450.49 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8020 mL	9.0098 mL	18.0196 mL
	5 mM	0.3604 mL	1.8020 mL	3.6039 mL
	10 mM	0.1802 mL	0.9010 mL	1.8020 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Rolapitant hydrochloride hydrate (SCH619734 hydrochloride hydrate) is a potent, selective, long-acting and orally active neurokinin 1 (NK1) receptor antagonist with a K_i of 0.66 nM. Rolapitant hydrochloride hydrate does not interact with CYP3A4. Rolapitant hydrochloride hydrate 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 hydrochloride hydrate 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 hydrochloride hydrate (1-1000 nM) inhibits the GR-73632 (an NK1 receptor agonist)-induced calcium efflux in 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 hydrochloride hydrate (0.03-1 mg/kg for PO, 0.3-1 mg/kg for IV; single dosage) attenuates the GR-73632 (HY-

P1192)-induced foot-tapping response in Mongolian Gerbils[1].
Rolapitant hydrochloride hydrate (0.03-1 mg/kg; PO; single dosage; observed for 72 h) blocks acute emesis induced by both apomorphine and cisplatin (HY-17394) 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]. 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.

[2]. 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.

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