MK-0249

Cat. No.: HY-U00076

CAS No.: 862309-06-6

Molecular Formula: $C_{23}H_{24}F_3N_3O_2$

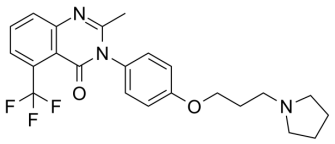
Molecular Weight: 431.45

Target: Histamine Receptor

Pathway: GPCR/G Protein; Immunology/Inflammation; 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 : 50 mg/mL (115.89 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3178 mL	11.5888 mL	23.1777 mL
5 mM	0.4636 mL	2.3178 mL	4.6355 mL
10 mM	0.2318 mL	1.1589 mL	2.3178 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: ≥ 1.25 mg/mL (2.90 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.90 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description MK-0249 (Compound 1) is a potent, selective and orally active histamine H_3 receptor antagonist, with an IC_{50} of 1.7 nM for human H3[1].

IC_{50} & Target	human H_3 receptor	rhesus H_3 receptor	human H_3 receptor	rat H_3 rece
	1.7 nM (IC_{50})	4.3 nM (Ki)	6.8 nM (Ki)	33 nM (Ki)

In Vitro MK-0249 (Compound 1) shows very good hepatic clearance values (CLh e 11 mL/min/kg), and is a substrate for rat P-gp but not for human P-gp[1].
MK-0249 displays potent binding affinity to human, rat, and rhesus H_3 receptors with K_i values of 6.8 ± 1.3 nM, 33 ± 3 nM, and 4.3 ± 1.2 nM, respectiv

MK-0249 shows high intrinsic activity[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

MK-0249 (Compound 1) (0-30 mg/kg; p.o.; once) elevates histamine levels in the rat brain in a dose-dependent manner[1].

MK-0249 (10 mg/kg; p.o.; once) shows markedly higher brain penetrability and a lower plasma Occ90 value in mdr1a (-/-) mice than in mdr1a (+/+) m

MK-0249 shows rodent brain permeability and is significantly limited by P-gp mediated efflux in rodents, whereas the extent of P-gp mediated efflu small or negligible[1].

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Animal Model:	SD rats[1]
Dosage:	3, 10 and 30 mg/kg
Administration:	Oral administration, once
Result:	Showed a statistically significant increase in tele-methylhistamine levels at 30 mg/kg.

Animal Model:	P-gp-deficient mdr1a (-/-) and wild type mdr1a (+/+) CF-1 mice[1]
Dosage:	10 mg/kg
Administration:	Oral administration, once
Result:	The brain-to-plasma ratio in mdr1a (-/-) mice (b/p = 14) was remarkably higher than that in SD rats (b/p = 1.1 (b/p = 0.8).

Animal Model:	Male Sprague-Dawley rats, male Beagle dogs, and male rhesus monkeys[1]
Dosage:	1 or 3 mg/kg
Administration:	IV or PO (Pharmacokinetic Analysis)
Result:	Pharmacokinetic Parameters of 1 in Rats, Dogs, and Rhesus Monkeys[a][1]

		iv (1 mg/kg)			po (3 mg/kg)		
	CL_p (mL/min/kg)	V_{dss} (L/kg)	$t_{1/2}$ (h)		C_{max} (μM)	$AUC_{0-\infty}$ (μM h)	F[b] (%)
rat	12	4.4	5.5		1.01	6.35	65
dog	19	9.7	9.9		1.8	11.8	>100

REFERENCES

[1]. Nagase T, et al. Synthesis, structure-activity relationships, and biological profiles of a quinazolinone class of histamine H3 receptor inverse Aug 14;51(15):4780-9.

McePdfHeight

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

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