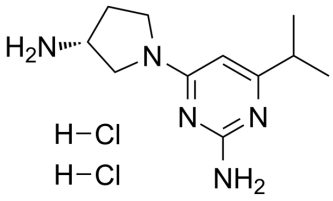
JNJ-39758979 dihydrochloride

Cat. No.:	HY-101189B
Molecular Formula:	$C_{11}H_{21}Cl_2N_5$
Molecular Weight:	294.22
Target:	Histamine Receptor
Pathway:	GPCR/G Protein; Immunology/Inflammation; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

JNJ-39758979 dihydrochloride is a selective, orally active, and high-affinity histamine H_4 receptor antagonist, with K_is of 12.5, 5.3, and 25 nM for human, mouse, and monkey histamine H_4 receptor, respectively. JNJ-39758979 dihydrochloride functionally antagonizes histamine-induced cAMP inhibition with a pA2 of 7.9 in transfected cells. JNJ-39758979 dihydrochloride shows good anti-inflammatory and antipruritic activity[1][2].

IC_{50} & Target

Human H_4 Receptor 12.5 nM (Ki)	Mouse H_4 Receptor 5.3 nM (Ki)	Monkey H_4 receptor 25 nM (Ki)	Rat H_4 receptor 188 nM (Ki)
Guinea pig H_4 receptor 306 nM (Ki)			

In Vitro

JNJ-39758979 dihydrochloride is a selective, high-affinity histamine H_4 receptor antagonist with a K_i of 12.5 nM versus the human H_4 receptor and functionally antagonizes histamine-induced cAMP inhibition with a pA2 of 7.9 in transfected cells. At the mouse H_4R, the K_i=5.3 nM and the pA2=8.3. At the monkey H_4R, the K_i=25 nM and the pA2=7.5. The affinity for the rat (K_i =188 nM, pA2 = 7.2) and guinea pig H_4R (K_i=306 nM) is moderate, and JNJ-39758979 dihydrochloride has little if any affinity for the dog H_4R (K_i≥10 μM). The compound is highly selective for H_4R, as it exhibits low affinity for the H_1, H_2, and H_3 receptors[1].

JNJ-39758979 dihydrochloride is metabolically stable ($t_{1/2}$ >120 min) when incubated in vitro with human, rat, dog, or monkey liver microsomes[1].

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

In Vivo

JNJ-39758979 dihydrochloride (10 mg/kg; p.o.) treatment shows that the C_{max}, $t_{1/2}$ and F values are 0.3 μM, 7.5 hours, 36%, respectively[1].

JNJ-39758979 dihydrochloride (2 mg/kg; i.v.) treatment shows that the Vss, AUC, CL and $t_{1/2}$ were 19.9 L/kg, 1.4 μM*h, 2.2 L/h, and 2.1 hours, respectively [1].

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

Animal Model:	Sprague-Dawley rats[1]
Dosage:	10 mg/kg
Administration:	Oral administration (Pharmacokinetic Analysis)

Result:	The C_{max}, $t_{1/2}$ and F values were 0.3 μM, 7.5 hours, and 36%, respectively.

REFERENCES

[1]. Savall BM, et al. Discovery and SAR of 6-alkyl-2,4-diaminopyrimidines as histamine H_4 receptor antagonists. J Med Chem. 2014 Mar 27;57(6):2429-39.

[2]. Murata Y, et al. Phase 2a, randomized, double-blind, placebo-controlled, multicenter, parallel-group study of a H4 R-antagonist (JNJ-39758979) in Japanese adults with moderate atopic dermatitis.

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