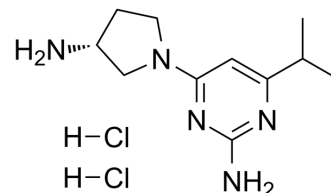


JNJ-39758979 dihydrochloride

Cat. No.:	HY-101189B
Molecular Formula:	C ₁₁ H ₂₁ Cl ₂ N 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	<p>JNJ-39758979 dihydrochloride is a selective, orally active, and high-affinity histamine H₄ receptor antagonist, with K_is of 12.5, 5.3, and 25 nM for human, mouse, and monkey histamine H₄ 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]}.</p>									
IC₅₀ & Target	Human H ₄ Receptor 12.5 nM (K _i)	Mouse H ₄ Receptor 5.3 nM (K _i)	Monkey H ₄ receptor 25 nM (K _i)	Rat H ₄ receptor 188 nM (K _i)						
	Guinea pig H ₄ receptor 306 nM (K _i)									
In Vitro	<p>JNJ-39758979 dihydrochloride is a selective, high-affinity histamine H₄ receptor antagonist with a K_i of 12.5 nM versus the human H₄ receptor and functionally antagonizes histamine-induced cAMP inhibition with a pA₂ of 7.9 in transfected cells. At the mouse H₄R, the K_i=5.3 nM and the pA₂=8.3. At the monkey H₄R, 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 H₄R (K_i=306 nM) is moderate, and JNJ-39758979 dihydrochloride has little if any affinity for the dog H₄R (K_i≥10 μM). The compound is highly selective for H₄R, as it exhibits low affinity for the H₁, H₂, and H₃ receptors^[1].</p> <p>JNJ-39758979 dihydrochloride is metabolically stable (t_{1/2} >120 min) when incubated in vitro with human, rat, dog, or monkey liver microsomes^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>									
In Vivo	<p>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].</p> <p>JNJ-39758979 dihydrochloride (2 mg/kg; i.v.) treatment shows that the V_{ss}, 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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1" data-bbox="341 1743 1510 1921"> <tr> <td>Animal Model:</td> <td>Sprague-Dawley rats^[1]</td> </tr> <tr> <td>Dosage:</td> <td>10 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>Oral administration (Pharmacokinetic Analysis)</td> </tr> </table>				Animal Model:	Sprague-Dawley rats ^[1]	Dosage:	10 mg/kg	Administration:	Oral administration (Pharmacokinetic Analysis)
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 μ M, 7.5 hours, and 36%, respectively.

REFERENCES

- [1]. Savall BM, et al. Discovery and SAR of 6-alkyl-2,4-diaminopyrimidines as histamine H₄ 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 H₄R-antagonist (JNJ-39758979) in Japanese adults with moderate atopic dermatitis.
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Caution: Product has not been fully validated for medical applications. For research use only.

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