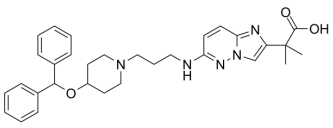
Bamirastine

Cat. No.:	HY-101601
CAS No.:	215529-47-8
Molecular Formula:	$C_{31}H_{37}N_5O_3$
Molecular Weight:	527.66
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	Bamirastine inhibits ligand binding to recombinant human histamine H_1 receptors (rhH_1R) with an IC_{50} value of 17.3 nM.
IC_{50} & Target	IC50: 17.3 nM (rhH_1R)[1]
In Vitro	Bamirastine (TAK-427) reduces specific binding of [^{3}H] pyrilamine to recombinant human H_1 receptors (rhH_1R) is seen in a concentration- dependent manner with an IC_{50} value of 17.3 nM. The K_i value is calculated to be 7.35 nM. The affinity of Bamirastine is found to be as high as that of azelastine, 2 times lower than that of Epinastine, 8 times lower than that of ketotifen and 3 times higher than that of Terfenadine[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Bamirastine (TAK-427) inhibits histamine induced skin reactions in guinea pigs and mice with an ID_{50} value of 0.884 and 0.450 mg/kg, p.o., respectively; significant inhibition associated with 10 mg/kg of Bamirastine is still observed 24 h after dosing in guinea pigs. Even at 300 mg/kg, Bamirastine does not affect pentobarbital-induced sleeping time in mice. Bamirastine significantly inhibits passive cutaneous anaphylaxis (PCA) in mice and guinea pigs, and also inhibits antigen-induced ISRs in guinea pigs[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

The binding assay is performed using 96 well microplates, and 50 mM Tris-HCl containing 0.1% BSA, pH 7.4 is used as the assay buffer. Various concentrations of test compounds (50 µL/well), [^{3}H] pyrilamine (22 nM, 25 µL/well, final 2.75 nM) and promethazine (80 µM, 25 µL/well, non-specific binding) or equal volumes of assay buffer are mixed, and the binding assay is initiated by the addition of the membrane suspension (5 µg protein/100 µL/well). The mixtures are incubated for 1 h at room temperature and the incubation is terminated by filtration over 0.3% polyethyleneimine treated Unifilter^{TM} plates GF/C using a harvester. The UnifilterTM-plates are washed 3 times with 50 mM Tris-HCl buffer, pH 7.4, and dried completely. The radioactivity is counted by a TopCount system. Specific binding is defined as radioactivity bound after subtraction of nonspecific binding determined in the presence of promethazine. A K_i value (nM) is calculated, In order to characterize the inhibition of the H_1 receptor binding by Bamirastine (TAK-427), saturation curves for specific binding of [^{3}H] pyrilamine to the membranes expressing human histamine H_1 receptors are investigated in the absence and presence of Bamirastine at 10 and 30 nM. The binding parameters are calculated from the Scatchard analysis of the saturation curves[1].

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Animal Administration [1]	Mice[1] Male Crj: ICR mice (5 weeks old) are used. Bamirastine, Terfenadine and Epinastine in doses of 30, 100 and 300 mg/kg or vehicle (0.5% methylcellulose) are given orally. Behavior is observed for the first 2 h after drug administration. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Fukuda S, et al. Characteristics of the antihistamine effect of TAK-427, a novel imidazopyridazine derivative. Inflamm Res. 2003 May;52(5):206-14.

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