Product Data Sheet

Product Name: Bamirastine (TAK-427)
Cat. No.: GC31840

Chemical Properties

Cas. No.	215529-47-8		
SMILES	O=C(O)C(C)(C)C1=CN2N=C(NCCCN3CCC(OC(C4=CC=CC=C4)C5=CC=CC=C5)CC3)C=CC2=N1		
Formula	$C_{31}H_{37}N_5O_3$	M.Wt	527.66
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Bamirastine (TAK-427)		

Protocol

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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Kinase experiment:

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), [3H] 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 UnifilterTM 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 Ki value (nM) is calculated, In order to characterize the inhibition of the H1 receptor binding by Bamirastine (TAK-427), saturation curves for specific binding of [3H] pyrilamine to the membranes expressing human histamine H1 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].

Animal experiment:

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.

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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.

Background

Bamirastine inhibits ligand binding to recombinant human histamine H1 receptors (rhH1R) with an IC50 value of 17.3 nM.

Bamirastine (TAK-427) reduces specific binding of [3H] pyrilamine to recombinant human H1 receptors (rhH1R) is seen in a concentration- dependent manner with an IC50 value of 17.3 nM. The Ki 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].

Bamirastine (TAK-427) inhibits histamine induced skin reactions in guinea pigs and mice with an ID50 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].

[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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