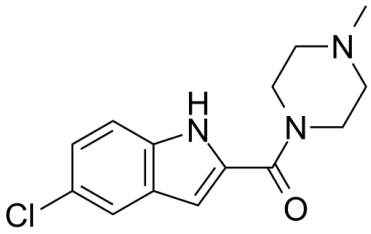
Data Sheet

Product Name:	JNJ-7777120
Cat. No.:	CS-4964
CAS No.:	459168-41-3
Molecular Formula:	C14H16ClN3O
Molecular Weight:	277.75
Target:	Histamine Receptor
Pathway:	GPCR/G Protein; Immunology/Inflammation; Neuronal Signaling
Solubility:	DMSO : ≥ 50 mg/mL (180.02 mM)



BIOLOGICAL ACTIVITY:

JNJ-7777120 is a selective H4R antagonist with Ki of 4 ±1 nM, exhibits >1000-fold selectivity over the other histamin receptors. IC50 value: 4 ±1 nM (Ki) [1] Target: histamine H4 receptor in vitro: JNJ-7777120 prevents fibronectin-induced lung fibroblast migration, thus suggesting that H4R could represent an attractive target for the development of new drugs for lung fibrosis treatment .[2] in vivo: JNJ 7777120 blocks histamine-induced chemotaxis and calcium influx in mouse bone marrow-derived mast cells. In addition, it can block the histamine-induced migration of tracheal mast cells from the connective tissue toward the epithelium in mice. JNJ 7777120 significantly blocks neutrophil infiltration in a mouse zymosan-induced peritonitis model. [3]

PROTOCOL (Extracted from published papers and Only for reference)

Kinase assay [3] A panel of 50 different biogenic amine receptors, neuropeptide receptors, ion channel binding sites, and neurotransmitter transporter binding assays were run. The targets run were: human adenosine A1, A2A, and A3 receptors; adrenergic receptors α1 (nonselective), α2 (nonselective), and β1; norepinephrine (NE) transporter; angiotensin II receptor (AT2); rat brain benzodiazepine receptor (BZD); bradykinin receptor 2 (B2); cholecystokinin receptor 1 (CCK1); dopamine D1 and D2 receptors; dopamine transporter (DA); endothelin receptor A (ETA); rat brain GABA receptor; galanin receptor 2 (GAL2); CXCR2; CCR1; vasopressin receptor 1A (V1A); melanocortin receptor 4 (MC4); chicken melatonin receptor 1 (MT1); muscarinic receptors M1, M2, and M3; neurokinin receptors 2 and 3 (NK2, NK3); neuropeptide receptors 1 and 2 (NPY1, NPY2); neurotensin receptor 1 (NT1); opioid receptors δ (DOP), κ (KOP), and μ (MOP); nociceptin receptor (ORL1); serotonin receptors 5-HT1A, 5-HT2A, 5-HT3, 5-HT5A, 5-HT6, 5-HT7, and rat 5-HT1B; rat σ receptor (SST); vasoactive intestinal peptide receptor 1 (VIP1); rat Ca2+ channel verapamil site; rat brain voltage-gated potassium channel (K+V channel); rat brain small-conductance Ca2+-activated K+ channel (SK+Ca channel); rat Na+ channel (site 2); and rat Cl- channel. All assays were run using recombinant human receptors, except where noted. The assays were run at 1 μM of JNJ 7777120, and the percentage of inhibition is given as the average of three determinations. Animal administration [3] Mice (n = 10 per group) were dosed with either vehicle or JNJ 7777120 15 min before being challenged by a 20-min aerosol inhalation of 0.1 M histamine dihydrochloride or PBS. This was repeated for 2 days. JNJ 7777120 was administered at 20 mg/kg s.c. in 20% (w/v) hydroxypropyl-β-cyclodextrin. Four hours after the last challenge, animals were euthanized by pentobarbital overdose (i.p.) and severing of the abdominal aorta. Trachea were cleared of blood via perfusion of PBS/heparin through the right ventricle and fixed in 10% (w/v) formaldehyde (neutral buffered formalin) for subsequent paraffin cross-sectioning and toluidine blue staining.

References:

[1]. Jablonowski JA, et al. The first potent and selective non-imidazole human histamine H4 receptor antagonists. J Med Chem. 2003 Sep 11;46(19):3957-3960.

[2]. Rosa AC, et al. Prevention of bleomycin-induced lung inflammation and fibrosis in mice by naproxen and JNJ-7777120 treatment. J Pharmacol Exp Ther. 2014 Nov;351(2):308-316.

[3]. Thurmond RL, et al. A potent and selective histamine H4 receptor antagonist with anti-inflammatory properties. J Pharmacol Exp Ther. 2004 Apr;309(1):404-413.

CAIndexNames:

Methanone, (5-chloro-1H-indol-2-yl)(4-methyl-1-piperazinyl)-

SMILES:

O=C(C(N1)=CC2=C1C=CC(Cl)=C2)N3CCN(C)CC3

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