Target Name	Histamine H4 receptor
Target TTD ID	TTDR01193

Target Species	Human
Chemical Type	Quinazoline sulfonamides
Mode of Action	Inverse Agonist
QSAR Model 1	$\mathrm{p}K_i\mathrm{hH_4R} = 3.632(\pm 2.253) + 5.891(\pm 0.656)[\mathbf{aICM}] - 0.054(\pm 0.012)[\mathbf{PEOE\_VSA+5}]$ $-0.027(\pm 0.008)[\mathbf{SMR\_VSA1}] + 0.086(\pm 0.038)\ [\mathbf{PEOE\_VSA-3}]$ $+ 11.174(\pm 4.976)[\mathbf{GCUT\_PEOE\_1}] - 1.616(\pm 0.792)[\mathbf{PEOE\_VSA\_FPOS}]$ $N = 31, r = 0.918, R^2 = 0.842, S = 0.333, F_{6,24} = 21.302, F_{5\%,6,24} = 2.508, q^2 = 0.789$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** **a_ICM** : entropy of the element distribution in the molecule **PEOE_VSA+5** : sum of the van der Waals surface area of atoms, whose PEOE partial charge is between 0.25 and 0.30 **PEOE_VSA-3** : sum of the van der Waals surface area of atoms, whose PEOE partial charge is between -0.20 and -0.15 **PEOE_VSA_FPOS** : sum of the van der Waals surface area of atoms, whose PEOE partial charge is positive, divided by the total surface area **SMR_VSA1** : subdivided surface area descriptor based on the sum of the approximate accessible van der Waal's surface area, calculated for each atom with contribution to molar refractivity in the range of 0.11 to 0.26 **GCUT_PEOE_1** : descriptor calculated from the eigenvalues of a modified graph adjacency matrix. The diagonal of the matrix takes the value of the PEOE partial charges.

	Note - PEOE is a partial charge descriptor calculated using the partial equalization
Reference	Synthesis and QSAR of Quinazoline Sulfonamides As Highly Potent Human Histamine H4 Receptor Inverse Agonists. *J. Med. Chem*. 2010, 53, 2390–2400

Target Species	Human
Chemical Type	Clobenpropit analogs
Mode of Action	Dual activity ligand for H3 and H4 receptors
QSAR Model 1	$pK_i\ hH_4R = 17.215\ (\pm 6.451) + 0.030\ (\pm 1.277)\ [E\_sol \times 10^{-3}] + 4.849\ (\pm 1.224)\ [BCUT\_SLOGP\_0]$ $- 0.133\ (\pm 13.800)\ [GCUT\_PEOE\_1] + 4.199\ (\pm 3.455)\ [BCUT\_PEOE\_2]$ $N = 22, r = 0.748, R^2 = 0.560, S = 0.339, F_{4,17} = 5.413, F_{5\%,4,17} = 2.965.$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** BCUT_PEOE_2: A descriptor calculated from the eigenvalues of a modified distance adjacency matrix. The diagonal of the matrix takes the PEOEa partial charges (Steric, electrostatic); BCUT_SLOGP_0: A descriptor calculated from the eigenvalues of a modified distance adjacency matrix. The diagonal of the matrix takes the value of the atomic contribution to log P (Steric, hydrophobic); dipoleZ: The z component of the dipole moment (Electrostatic); E_sol: The solvation energy descriptor (Hydrophobic) E_stb: The bond stretch-bend cross-term potential energy descriptor calculated from stored 3D conformations (Steric); GCUT_PEOE_1: A descriptor calculated from the eigenvalues of a modified graph distance adjacency matrix. The diagonal of the matrix takes the value of the atomic contribution to molar refractivity (Steric, electrostatic); GCUT_SMR_2: A descriptor calculated from the eigenvalues of a modified graph distance adjacency matrix. The diagonal of the matrix takes the value of the atomic contribution to molar refractivity

	(Steric); SlogP_VSA3: The subdivided surface area descriptor based on the sum of the approximate accessible van der Waal's surface area, calculated for each atom with contribution to log of partition coefficient (octanol/water) in the range of 0–0.1 (Hydrophobic)
Reference	Clobenpropit analogs as dual activity ligands for the histamine H3 and H4 receptors: Synthesis, pharmacological evaluation, and cross-target QSAR studies. *Bioorganic & Medicinal Chemistry* 17 (2009) 3987–3994

Target Species	Human
Chemical Type	Indole derivatives
Mode of Action	Antagonist
QSAR Model 1	$$pK_i = 5.4572 - 0.0002(HF - 12.963)^2 - 0.0601(\log D_{1.5} + 5.758)^2 + 0.0191(\mu_x + 3.639)^2 - 0.3916(pI - 8.811)^2 - 1.3107qC5$$ $N = 25; r^2 = 0.76; q^2 = 0.60; LOF = 0.13; LSE = 0.07;$ outliers $= 0$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** HF is the heat or enthalpy of formation (thermodynamic descriptor); $\log D_{1.5}$ is the calculated n-octanol/water distribution coefficient in pH 1.5; μ_x is the dipole moment at x coordinate; pI_l is the isoeletric point; and qC5 is the ESP partial atomic charge of the carbon bound to the R5 substituent.
Reference	Molecular modeling and QSAR studies of a set of indole and benzimidazole derivatives as H4 receptor antagonists. *J Mol Model* (2011) 17:921–928

Target Species	Human
Chemical Type	Benzimidazole derivatives

Mode of Action	Antagonist
QSAR Model 1	$$pK_i = 5.4572 - 0.0002(HF - 12.963)^2 - 0.0601(\log D_{1.5} + 5.758)^2 + 0.0191(\mu_x + 3.639)^2 - 0.3916(pI - 8.811)^2 - 1.3107qC5$$ $N = 25; r^2 = 0.76; q^2 = 0.60; LOF = 0.13; LSE = 0.07;$ outliers $= 0$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** HF is the heat or enthalpy of formation (thermodynamic descriptor); $\log D_{1.5}$ is the calculated n-octanol/water distribution coefficient in pH 1.5; μ_x is the dipole moment at x coordinate; pI_l is the isoeletric point; and qC5 is the ESP partial atomic charge of the carbon bound to the R5 substituent.
Reference	Molecular modeling and QSAR studies of a set of indole and benzimidazole derivatives as H4 receptor antagonists. *J Mol Model* (2011) 17:921–928