Homology modelling and binding site mapping of the human histamine H1 receptor

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„...25] , 6.43 [25] 8.92 [26] 8.65 [26] 4.58 [26] , respectively). p K a values of acrivastine (2.82, 7.59) were calculated by **CompuDrug**'s Pallas software [27] . Before starting the docking procedure we represented the channel surfaces of our receptor model..."

Abstract

Three-dimensional model of the human histamine H1 receptor was developed by homology modelling using the high resolution structure of bovine rhodopsin as template. Genetic algorithm based docking calculations were used to identify the role of several amino acids having an effect on agonist or antagonist binding. Binding mode analyses of mepyramine, desloratidine, loratidine and acrivastine allowed us to rationalise their binding affinity. Binding site mapping resulted in seven new potential aromatic interaction points (Tyr 108, Phe 184, Phe 190, Phe 199, Phe 424, Trp 428, Tyr 431), that took part in forming the lipophilic pocket of the antagonist binding cavity.
Keywords: Human histamine H1 receptor; Homology model; Binding site mapping; Antagonist
Abbreviations: HHR1, human histamine H1 receptor; GPCR, G-protein coupled receptor; TM, transmembrane domain; BBB, blood brain barrier; EC, extracellular; IC, intracellular

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