Current Drug Discovery Technologies
2020 Apr 20.

In sillico analysis, synthesis, and biological evaluation of triazole derivatives as a H1 receptor antagonist

Sandip N Badeliya, Ishan I Panchal, Bibhranjan Panigrahi, C N Patel

Department of Pharmaceutical Chemistry, Saraswathi Institute of Pharmaceutical Sciences, Dhanap, Gandhinagar, Gujarat. India.
Department of Pharmaceutical chemistry, Parul Institute of Pharmacy, Parul University, Vadodara, Gujarat. India.
3Lupin Pharmaceuticals, Pune. India.
Department of Pharmaceutical chemistry, Shri Sarvajanik Pharmacy College, Mehasana, Gujarat. India.

Abstract: Background: Histamine, a biological amine, is considered as a principal mediator of many pathological processes regulating several essential events in allergies and autoimmune diseases. Numerous derivatives have been developed that strive with histamine at H1 receptor and prevent binding of histamine at H1 receptor thus prevent allergic reactions. Molecules containing triazole ring fused with six-membered ring systems are found to possess broad applications in the field of medicine and industry. The present study is an attempt to characterize the impact of the nature of the substituent introduced at the 5 positions of the-4H-1,2,4-triazole-3-thiol on their capacities to bind with H1 receptor.
Methods: Molecular docking (PDB ID: 3RZE) revealed that synthesized derivatives and target proteins were actively involved in binding with Tyr-108, Thr-112, Ala-216, and Phe432 subunits. The pharmacophore model new 5-(4-substituted phenyl)-4-(phenylamino)- 4-H-1,2,4-triazole-3-thiols (5a-5h) were designed and evaluated for H1-blocking activity using isolated segments from the guinea pig ileum.
Results: According to in silico analysis, all the compounds have a topological polar surface area (TPSA) less than 140 Å squared, so they tend to a good penetration in cell membranes. The results show that most of the compounds are non-inhibitors of CYP450 substrates that play a fundamental role in drug metabolism. Compounds 5d (50.53±12.03), 5h (50.62±12.33) and 7a (55.07±12.41) are more active than others.
Conclusion: Finally, these derivatives were screened for H1 receptor antagonist activity using guinea pig ileum taking chlorpheniramine maleate as a standard. Most of the compounds possesses better antihistamine activity.

Key words: 1; 2; 4-triazole; Histamine; Molecular docking; TPSA; guinea pig ileum; guinea pig ileum Histamine.

Link: https://www.eurekaselect.com/181114/article