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Research Article

Molecular Docking Study and Structure Based Design of Ketotifen and Some of its Analogues Including ADME and Toxicity Study

ABSTRACT

One of the most interesting drugs in the treatment of allergic reactions, especially asthma, is ketotifen, it is a benzocycloheptathiophene which shows clearly distinguishable anti-anaphylactic, antimediator and strong H1 receptor antagonism properties that results in moderate to marked improvement of symptoms in the majority of patients with asthma, dermatitis, seasonal or perennial rhinitis, allergic conjunctivitis, chronic or acute urticaria and food allergy. Ketotifen is available as an over the counter treatment for ocular allergy. In this study, we compared between ketotifen as a model for antihistamine and a series of its analogues, by docking and evaluation of their binding with certain receptors, including Dopamine D3 receptor (which is present in the brain and related to cognitive function and modulate memory, emotions and motivation), Histamine dehydrogenase enzyme (which is highly specific for histamine and catalyzes the oxidative deamination of histamine to imidazole acetaldehyde), Histidine triad nucleotide binding protein 1 (1avs), and Histidine triad nucleotide binding protein 1 (1kpf) HINT1 (which are belong to the histidine triad (HIT) family, a 126 amino acid proteins, these proteins bind zinc and purine nucleotides, then zinc ions mediate the interaction between HINT1 and third party proteins). Also we investigate enzymes activity on these compounds, toxicity, pharmacokinetics and physicochemical properties. Lipinski rule of five (Ro5) has been calculated, all theoretical products have been obey to Lipinski rule and best fit with specific receptors. According to the results we notice that the compounds sar2a, sar3a had the most promising results and they could have better activity than the original drug.