QSAR and Molecular Docking Studies on Phthalazinone Derivatives as H_1 and H_3 dual inhibitors: A New Approach to Treatment of Allergic Rhinitis

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Abastract: Dual target based drug design is a creative method for finding new medications that recently has been reported in several researches. Many considerable target has been suggested for this pathway that among them H1 and H3 histamine receptor was our purpose in this study. Both of them predominantly involved in allergic reactions. The main goal of this approach is the introduction of new more potent and selective case with fewer side effects than single target drugs. In this study QSAR, molecular docking and molecular dynamic simulations were employed for a series of H1 and H3 hybrid antagonists that have been reported recently for treatment of allergic rhinitis. The descriptors were calculated by DRAGON and HyperChem software. The final model was built by MATLAB and building mode of every antagonist was evaluated by molecular docking using AutoDokc4.2. The best QSAR models in MLR were reported, with the square correlation coefficient for H1 antagonist (0.937) and (0.987) for H3 antagonist. The high value of the correlation coefficients, indicate that the models were satisfactory. The created MLR Models also indicated the significance of MW, bulkiness, branching and flexibility of molecule in inhibitory activities against H1 and H3 receptors. The docking study indicated that the steric, electrostatic interactions and hydrophobic bunds in the active site of the histamine H1and H3-receptor are important and by the incorporation of these specifications with HB donor/acceptor groups, the molecules would have displays the important structural property that impact the inhibitory effect. The QSAR and docking analyses demonstrated to be helpful tools in the prediction of anti-histaminic activities and for provide more pharmacophor understanding that could be used to design new agents with more potent dual histamine receptors inhibitory activity.

Keyword: QSAR, Docking, Phthalazinone Derivatives, Allergic Rhinitis, Dual Inhibitors

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