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Molecular docking study on the interaction of human procalcitonin with 3-(1-(2-mercaptoethylamino)ethylidene)-chroman-2,4-dion

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Introduction

Coumarins or benzo-α-pirones are a very large and important class of heterocyclic compounds and have an important place in the chemistry of natural products. The structure of coumarin contains the fused pyrone and benzene rings along with the carbonyl group on the pyrone ring. Procalcitonin (~13 kDa) is a peptide consisting of 116 amino acids. Procalcitonin is enzymatically degraded into lower molecular weight peptides. The biological effect of this protein was proven in the study of Nyen et al. (1996) who showed that the elevated concentrations of Procalcitonin can lead to sepsis which can be treated with the anti- Procalcitonin antibodies.

Aim

In this contribution, the coumarine derivate 3-(1-(2-mercaptoethylamino) ethylidene)-chroman-2,4-dion, is investigated for the reactivity toward against human protein Procalcitonin by the means of Molecular Docking analysis. Molecular docking studies have proved as very important for the interactions of coumarine derivatives with biologically important proteins.

Methodology

Molecular docking analysis was carried out in order to identify the inhibition potency of the coumarin 3-(1-(2-mercaptoethylamino) ethylidene)-chroman-2,4-dion (ligand) against human protein, Procalcitonin. The ligand was prepared for docking by minimizing their energy using B3LYP-D3BJ/6-311+G(d,p) level of theory. The inhibition activity was obtained for ten conformations of ligands inside the protein. This study showed that the molecular docking analysis is a very important tool in the analysis of the interactions of biologically important molecules and human Procalcitonin, in this case.

Conclusion

To evaluate the inhibitory nature of 3-(1-(2-mercaptoethylamino) ethylidene)-chroman-2,4-dion against human protein Procalcitonin, the Molecular docking studies are performed. Results indicate that the ligand forms a stable complex with Procalcitonin, as evident from the binding energy (Δg_{bind} in kJ/mol). The most important interactions are H-bonds, alkyl-π, π-π and π-amide. These preliminary results suggest that the investigated ligand might exhibit inhibitory activity against Procalcitonin proteins.

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Results

The lowest values of ΔG_{bind} and K_i are found for conformation 1. By analyzing the position of active amino acids, it can be concluded that ligand binds at the catalytic site of substrates by weak non-covalent interactions. The most prominent are H-bonds, alkyl-π and π-π interactions. Alanin and glutamin in positions 28 and 35 in the primary structure of procalcitonin chain have a predominant role as active inhibition sites, regardless of the conformation of investigated ligands. ALA28 forms one H-bond (2.09 Å length) with N-H group of the ligand, while GLN35 forms one H-bond (2.81 Å length) with S-H group of the ligand. TYR33 forms weak π-π interactions with benzene ring of the ligand. On the other hand, MET36 forms alkyl-π interactions with pyron ring of the ligand. These preliminary results suggest that the investigated compound might exhibit inhibitory activity against procalcitonin.