Docking of New Arylidene-Thiazolidinediones in the PPARγ Target


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Introduction

Nine new 5-arylidene-3-benzyl-thiazolidine-2,4-diones having halide groups on their benzyl rings were synthesized and assayed in vivo to investigate their anti-inflammatory activities (Figure 1). These compounds showed a considerably biological efficacy when compared to the reference drug rosiglitazone, a potent and well-known agonist of the Peroxisome Proliferator Activated Receptor Gamma (PPARγ) target. The goal of this work was to perform a docking study of these arylidene-thiazolidinediones in the PPARγ target.

Results and Discussion

The structural optimization of the arylidene-thiazolidinediones were performed using the AM1 method implemented in the BioMedCache program. Then docking studies were made using the PPARγ target co-crystallized with the rosiglitazone. This complex was taken from the RCSB Protein Data Bank under the 2PRG code. The FlexX 7.2 Program was used, taking into account the ligand flexibility during all the calculations. The active site was defined as all atoms within a radius of 6.5Å from the co-crystallized rosiglitazone ligand. Additionally, the rosiglitazone ligand was re-docked in order to test the program protocol.

The docking of the arylidene-thiazolidinediones indicated that they exhibit substantial specific interactions with key residues located in the active site of the PPARγ structure, which corroborates with the hypothesis of these molecules being potential agonists of PPARγ. An important trend was observed between the docking scores and the anti-inflammatory activities of this set of molecules (Figure 2). The comparison between the polar interactions (hydrogen bonds) observed in the docking results for the arylidene-thiazolidinediones and the co-crystallized rosiglitazone revealed the intermolecular reasons for the higher anti-inflammatory activity of the ligand 11.

Conclusions

Docking calculations can give important contributions to the elucidation of the molecular reasons of the anti-inflammatory activity of this class of molecules.

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