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Abstract

Molecular Docking Analysis of Novel Thiourea Derivatives of Naproxen with Potential Anti-Inflammatory Activity †

Nikola Nedeljković [1], Vladimir Dobričić [2], Marina Mijajlović [1], Zorica Vujić [2] and Miloš Nikolić [1,*]

[1] Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, 34000 Kragujevac, Serbia
[2] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Belgrade, 11221 Belgrade, Serbia
* Correspondence: milos.nikolic@medf.kg.ac.rs
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Abstract: Administration of current non-steroidal anti-inflammatory drugs is often associated with serious adverse effects. Therefore, there is a constant need to develop new molecules with anti-inflammatory activity. On the other hand, thiourea derivatives of non-steroidal anti-inflammatory drugs demonstrated significant anti-inflammatory activity in numerous studies. To clarify anti-inflammatory mechanism of action, in silico study was performed on four thiourea derivatives of naproxen, which were selected from the initial group of compounds synthesized by our research group. Tested compounds contain *p*-fluoroaniline (16), *p*-methoxyaniline (17), *p*-ethoxyaniline (18) and aniline (19) in the side chains. Selected 3D structures of enzymes COX-2 (3NT1) and 5-LOX (6NCF) were taken from PDB database. MAKE Receptor 3.2.0.2 software (OpenEye Scientific Software, Inc, Santa Fe, NM, United States) was used for preparation of enzymes' active sites, while ligands were prepared in OMEGA 2.5.1.4. FRED 3.2.0.2 software (OpenEye Scientific Software, Inc, Santa Fe, NM, United States) was employed for the analysis of binding poses into enzymes' active sites. All tested compounds showed key binding interactions with both enzymes. The highest number of key binding interactions was observed during molecular fitting of derivative 19 into the active site of COX-2 and derivatives 16 and 18 into the 5-LOX. Derivative 17 had the lowest value of free binding energy for both target enzymes (−14.90 kcal/mol for COX-2 and −9.57 kcal/mol for 5-LOX). Therefore, all analyzed compounds represent potential dual inhibitors of mentioned enzymes.

Keywords: thiourea; naproxen; COX-2; 5-LOX; molecular docking; FRED

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