Molecular docking analysis of novel thiourea derivatives of naproxen with potential antitumor activity

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INTRODUCTION

In the past few decades, thiourea derivatives have been intensively investigated as potential anticancer drugs [1]. This class of compounds has been recognized as agents with promising inhibitory activity towards human lung adenocarcinoma cell lines, human breast cancer cells and human colorectal carcinoma [2,3]. Antitumor activity of thiourea derivatives is based on potential inhibition of protein tyrosine kinases [4], topoisomerases [5] and carbonic anhydrase [6].

THE AIM OF THE STUDY

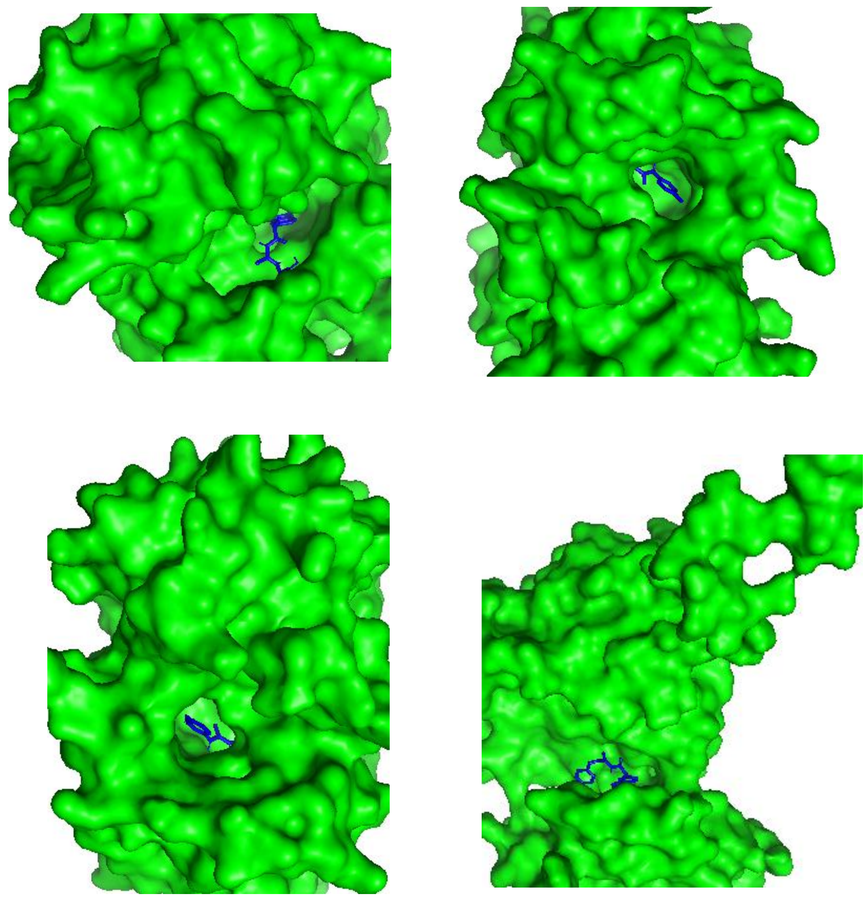
The aim of this study was to estimate antitumor potential of twenty newly designed thiourea derivatives of naproxen based on inhibition of selected protein kinases involved in multidrug resistance. Molecular docking analysis of these compounds was performed in two docking software packages in order to propose their potential mechanisms of action. Designed derivatives contain amino acids, esters of amino acids and aromatic amines in the side chains.

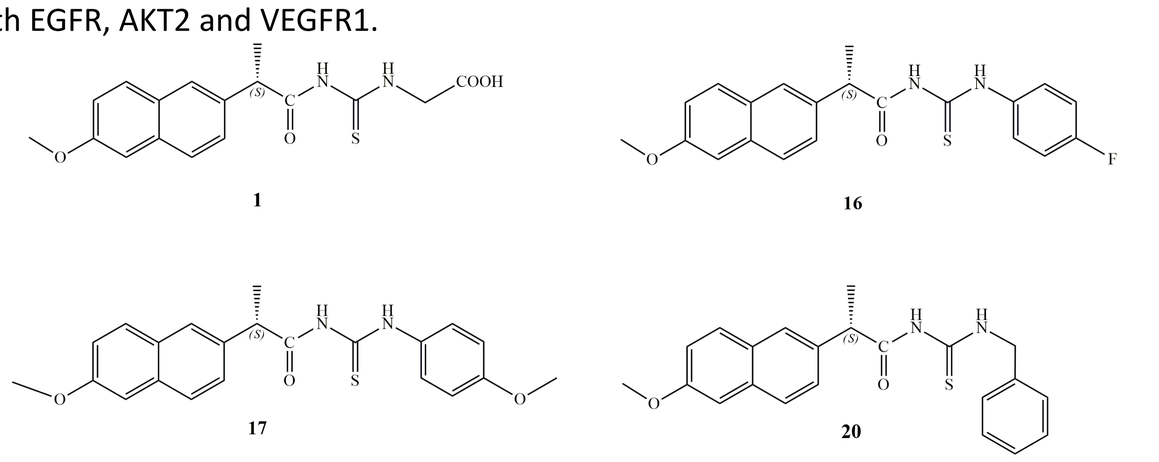
METHODS

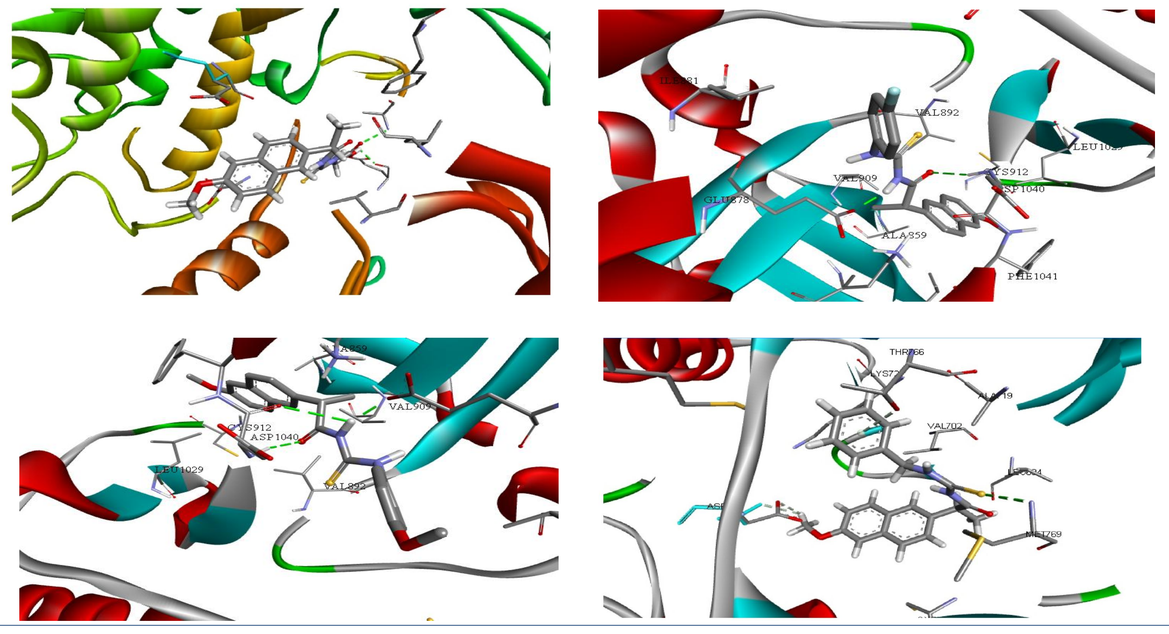
The FRED 3.2.0.2 [7-9] and AutoDock Vina [10] software were used for the analysis of binding of designed compounds into the active sites of the selected protein kinases: **EGFR** (PDB ID: 1M17), **AKT2** (PDB ID: 3E87), **VEGFR1** (PDB ID: 3HNG) and **mTOR** (PDB ID: 4JSV).

RESULTS

Analysis of binding poses in FRED software revealed the key binding interactions for derivatives **1** (with AKT2 and mTor) and **20** (with EGFR and VEGFR1). In AutoDock Vina derivatives **16** and **17** formed key binding interactions with EGFR, AKT2 and VEGFR1.







CONCLUSION

These 4 derivatives possess good molecular docking rankings in both docking software and represent potential anticancer candidates capable of fighting multidrug-resistant tumors.

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6th International Electronic Conference on Medicinal Chemistry
1-30 November 2020
sponsored: MDPI pharmaceuticals