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New Diagnostic and Therapeutic Tools against Multidrug Resistant Tumours

ABSTRACT BOOK

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Design of novel thiourea derivatives of naproxen with potential antitumor activity

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In the search for potent biologically active molecules, thiourea and other structure-related derivatives such as thiosemicarbazones have attracted great attention. In the past two decades, thiourea derivatives have been recognized as promising class of anticancer drugs due to their inhibitory activity against various targets, such as protein kinases and topoisomerases [1,2]. In this work, molecular docking analyses were performed on 20 thiourea derivatives of naproxen, previously designed by our group, in order to find their potential mechanisms of action. Designed derivatives contain amino acids and aromatic amines in the side chains. Following 3D structures of selected protein kinases involved in multidrug resistance were taken from PDB: 1M17 (EGFR), 3E87 (AKT2), 3HNG (VEGFR1) and 4JSV (mTOR). The receptor sites were prepared using MAKE Receptor 3.2.0.2 software [3]. Ligands were prepared in OMEGA 2.5.1.4 [4,5] and multiconformational binary files were generated. The FRED 3.2.0.2 software [6-8] was used for the analysis of binding poses into the receptor sites. The key binding interactions were observed for derivatives **1** (with AKT2 and mTor) and **20** (with EGFR and VEGFR1). Therefore, these derivatives possess the best multitarget potential and represent potential candidates for targeting multidrug resistant tumors (**Figure 1**).

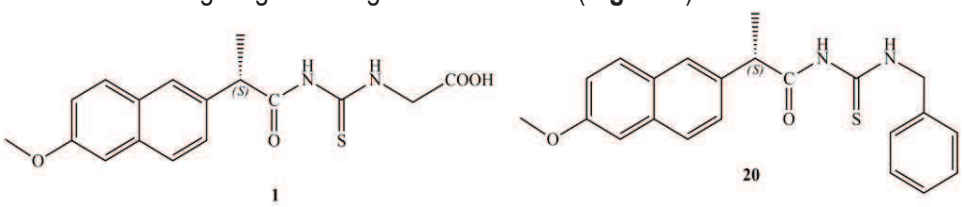

Figure 1. Chemical structures of **1** and **20.**

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