Molecular docking and 3D-QSAR analysis of newly synthetized and selected natural styryl lactones with antitumor activity

V. Vukic[1], D. Loncar[1], D. Vukic[1], L. Jevric[1], V. Popsavin[2]

[1]University of Novi Sad, Faculty of Technology Novi Sad, Bulevar cara Lazara 1, 21000 Novi Sad, Serbia,
[2]University of Novi Sad, Faculty of Sciences, Department of Chemistry, Biochemistry and Environmental Protection, Trg Dositeja Obradovića 3, 21000 Novi Sad, Serbia, **vukicv@tf.uns.ac.rs**

Styryl lactones are bioactive compounds with significant cytotoxicity against several tumour cell lines [1,2]. Due to its antiproliferative properties much attention was focused on the synthesis of novel styryl lactones derivatives. Prediction of cytotoxic and antiproliferative activity is a very important step in synthesis of compounds with desired biological activity [3,4]. Three-dimensional quantitative structure-activity relationship (3D-QSAR) and molecular docking simulations (that predicts the predominant binding orientation of a ligand to a target protein and estimates the relative strength of binding) were successfully used for this purpose [5,6]. *In vitro* cytotoxicity of analogues of (+)-goniofufurone and 7-*epi*-(+)-goniofufurone, as well as the synthesized styryl lactones containing the cinnamic acid ester groups were evaluated. From twenty four compounds six of them showed satisfactory to moderate inhibitory activity. These compounds have high docking scores and are able to make coordinative covalent bond with Fe2+ present in the active site of Cytochrome P450 17A1 receptor. Three-dimensional quantitative structure-activity relationship (3D-QSAR) model was established using the comparative molecular field analysis (CoMFA and CoMSIA) method. According to the obtained results steric field feature on the cinnamic acid ester groups at C-7 is crucial for the cytotoxic activity. This research suggests that the obtained 3D-QSAR model is able to successfully identify styryl lactones that have significant cytotoxic activity and provide information for screening and design of novel Cytochrome P450 17A1 inhibitors that could be used as drugs in treatment of prostate cancer.

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