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IN SILICO EVALUATION OF NEW POTENTIAL TARGET PROTEINS OF FLAVONOLIGNANS FROM SILYBUM MARIANUM

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The medicinal plant *Silybum marianum* (milk thistle) has been used from antiquity for treatment of liver and gallbladder disorders of different etiologies. Its main active component, silybin, occurs in two diastereoisomeric forms, silybin A and B. Silybin has been shown to exert a broad spectrum of bioactivities including cardioprotective, neuroprotective, antidiabetic and anticancer activities; however, the mechanisms of these actions have not been elucidated yet. In the current study, we assessed the chemical similarity of the silybin diastereoisomers to all approved drugs in the DrugBank database using ROCS software. Tanimoto Combo index, taking into account features obtained by shape and chemistry alignment of the compounds, was used as similarity estimator. The drugs scored with Tanimoto Combo indices ≥0.9 (9 drugs for silybin A and 9 drugs for silybin B) were filtered and analyzed in terms of target pathology and mechanisms of action. Among them three drugs exert antidiabetic (canaglifozin, dapaglifozin, empaglifozin) and two other drugs possess antitumor activities (vemurafenib and vismodegib). Since silybins have been reported to possess antitumor activities, the similarity with these drugs is of a particular interest when studying their mechanism of action. Since the X-ray structures of the antitumor drug targets, Smoothened homolog (vismodegib) and BRAF kinase (vemurafenib) are available, further docking studies of silybins in these receptors were performed and the possibility of silybin interactions with them was estimated. The results suggest that silybins can be accommodated in the binding sites of BRAF kinase and Smoothened homolog performing specific interactions with particular residues, including also those vemurafenib and vismodegib interact with. Experimental studies are necessary to prove the hypothesis that silybins can act as inhibitors of these proteins.

Recent Publications

1. Diukendjieva A, Al Sharif M, Alov P, Pencheva T, Tsakovska I, Paeva I (2017) ADME/Tox Properties and Biochemical interactions of Silybin Congeners: *In Silico* Study. Natural Product Communications, 12, 2.

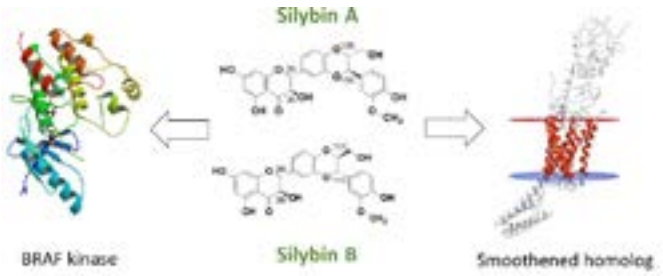

Figure 1. *In silico* evaluation of of silybin interactions with new potential target proteins based on similarity with their ligands

Biography

Antonia Diukendjieva got her BS Degree in Biotechnology and MS Degree in Biochemistry from Sofia University "St. Kliment Ohridski", Faculty of Biology. Currently she is a PhD student at the Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences. Her main scientific interests are in the field of Predictive Toxicology and *In Silico* Drug Design. Her most recent investigations relate to pharmacokinetic and pharmacodynamic evaluation of naturally-derived flavonoids.

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