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Nutraceutical search through the pipeline of pharmacophore-based virtual screening

Amit Dubey [1,2,3], Eugenio Del Prete [1,4], Serena Dotolo [1,5], Angelo Gaeta [1], Anna Marabotti [1,6], Pramod W. Ramteke [2] and Angelo Facchiano [1,*]

1: Istituto di Scienze dell'Alimentazione – CNR, via Roma 64 – Avellino-83100 (Italy)
2: Jacob School of Biotechnology and Bioengineering, Sam Higginbottom Institute of Agriculture, Technology and Sciences, Allahabad- 211007 (India)
3: International Centre for Genetic Engineering and Biotechnology, AREA Science Park Padriciano 99, Trieste-34149 (Italy)
4. Department of Sciences, University of Basilicata, Via Dell'Ateneo Lucano 10, 85100, Potenza (Italy)
5. Second University of Naples, Via Antonio Vivaldi, 43, 81100 Caserta (CE), (Italy)
6: Dipartimento di Chimica e Biologia "A. Zambelli", Università degli Studi di Salerno, Via Giovanni Paolo II 132, Fisciano-84084 (SA) (Italy)
**: corresponding author*
amit.dubey@isa.cnr.it, eugenio.delprete@isa.cnr.it, serenadotolo@unina2.it, angelo.gaeta.ag@gmail.com, amarabotti@unisa.it, pwramteke@yahoo.com, angelo.facchiano@isa.cnr.it

Nutraceuticals are food or their parts, present in conventional or non-conventional form, with verified safety and health benefits, beyond their nutritional value. In this work, we describe a novel pipeline for nutraceutical compounds research in the field of pharmacophore screening, providing a new idea for drug discovery. In the first step, to identify novel nutraceuticals potentially active as inhibitors of a given enzyme, a pharmacophore model is generated, with its key chemical features, starting from the experimental structure of the complex with known protein inhibitors, with pharmacophores ranking based on statistical values of sensitivity and specificity. After the validation step, this pharmacophore model is used for 3D structural screening and mapping against a subset of known nutraceutical compounds, generated through DrugBank or against special subsets from ZINC (ZINC Drug Database - Zdd and ZINC In Man - Zim). Moreover, molecular docking is performed to verify binding affinity of compounds. The hits with a good binding energy are then investigated in more details, compared with their pharmacophore features and analysed for their interacting residues. Then, to have an *in silico* interpretation of the potential activity of the compounds, an integrated investigation is performed, by mining literature reports about the effects of the specific compound (or food containing it) against human diseases, extracting expression data from omics repositories, in the view of integrating these information with molecular pathways and networks. Output of our pipeline are candidates for *in vitro* and *in vivo* experiments, to test the hypothesis and verify if they could become novel potential drugs.

Keywords: Pharmacophore, Virtual Screening, Dietary supplement, Nutraceutical, pharmacology, docking