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# Drug discovery by integration of pharmacophore modeling, virtual screening and biological evaluation by means of bioinformatics resources

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Drug discovery is a step-by-step process very important in biopharmaceutical field. We are interested in identifying new investigational *drug-likes* as potential inhibitors of determinate biological-therapeutic targets, trying to decrease the side effects and to safeguard the human health [1-2]. However, it is a long and very expensive process [3]. Therefore, we are using a new computational strategy, based on *Pharmacophore modeling*, to select bioactive substances (natural or synthetic), through the integration of bioinformatics online tools and local resource and platforms, in order to include into the strategy also knowledge from high-throughput studies, for new potential *lead compounds* generation-optimization, trying to accelerate the early phase of the drug development process [4].
The protocol of this new computational strategy is characterized by a multi-step design focused on: 1) *screening in RCSB-PDB for a crystal structure of a specific biological target*, suitable for the following steps; 2) *pharmacophore modeling and virtual computational screening*, by using public domain databases of bioactive compounds, as the ZINC[12] database [5], in order to find a promising molecule that could become a new potential medicine. 3) *molecular and biological evaluation*, to check the compounds selected by virtual screening, for their biological properties through public databases, as PubChem Compound, SciFinder, and Chemicalize to trace their origin and underline their most important physical-chemical features, PathPred (an enzyme-catalyzed metabolic pathway predictor server) to highlight and identify their biosynthetic-metabolic pathways and investigating the biotransformation of best candidates, analyzing their metabolites and their potential biological activity. Moreover, ADMET/toxicity predictor server applying the Lipinski-Veber filter are used to calculate the bioavailability the ADMET/toxicity properties.
After this check, only molecules with good bioavailability, good predicted activity and good ADMET properties are considered as hits compounds or *drug-likes* to direct the design of next experimental assays [6]. Finally, the lead compounds selected are analyzed through *molecular dynamics simulations.* 4) *simulations of molecular dynamics on the best lead compounds*, to investigate atomic details of protein-compound molecular interactions in different conditions (different organic solutions, organisms and systems).

## REFERENCES

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