A Study of Molecular Descriptor to Rank Candidate Ligands to Inhibit the InhA Receptor

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Background
In Rational Drug Design (RDD) [1], the interaction between receptor and ligands is the fundamental principle. In in-silico molecular docking experiments it is investigated the best bind and conformation of a ligand into a receptor [2]; those ligands that obtained better in-silico results are tested by in-vitro experiments; if results are promising, a new drug can be produced. However, currently there are more than 20 millions of small molecules available in repositories [3]. If considering the receptor flexibility, it is very expensive and time-consuming to test all these ligands with a single target protein. One possible strategy is to search ligand libraries and, based on a given criterion, select the most promising. In this work we are interested in select candidate ligands to inhibit the InhA [4] receptor from M. Tuberculosis.

Results
To reduce the time of ligand selection, some works have developed methods using the pharmacokinetic properties to filter the candidate ligands to drugs. For instance, Lipinski [5] introduced a set of parameters (rule of 5) capable of filtering ligands that have weak absorption, distribution, metabolism, excretion and toxicity (ADME/T), classifying them as drugs or non-drugs. But these rules have several exceptions and their classification does not guarantee that a particular molecule is drug or non-drug [6]. To improve the found results, we also must consider molecules pharmacodynamics properties. Hence we are motivated in applying molecular descriptors to filter and select this large amount of ligands to inhibit the InhA enzyme. Molecular descriptors [7] are numeric values that characterize molecules features, as physical-chemical properties. We studied six public ligand databases: Zinc, ChemDB, ChemSpider, ChemBank, PubChem and MMsINC, and its respective descriptors. Among them, we are looking for the best set of descriptors. Based on this study we fell encouraged to develop a ligand similarity heuristic function using molecular descriptors. Such function can generate a ranking of the most promising drug candidate molecules for the InhA receptor.

Conclusions
We proposed an application of molecular descriptors filters to rank ligand databases. We studied six distinct databases and analyzed them in terms of their molecular descriptors. We aim to develop a ligand similarity heuristic function to rank the most promising drug candidates for InhA receptor.

References