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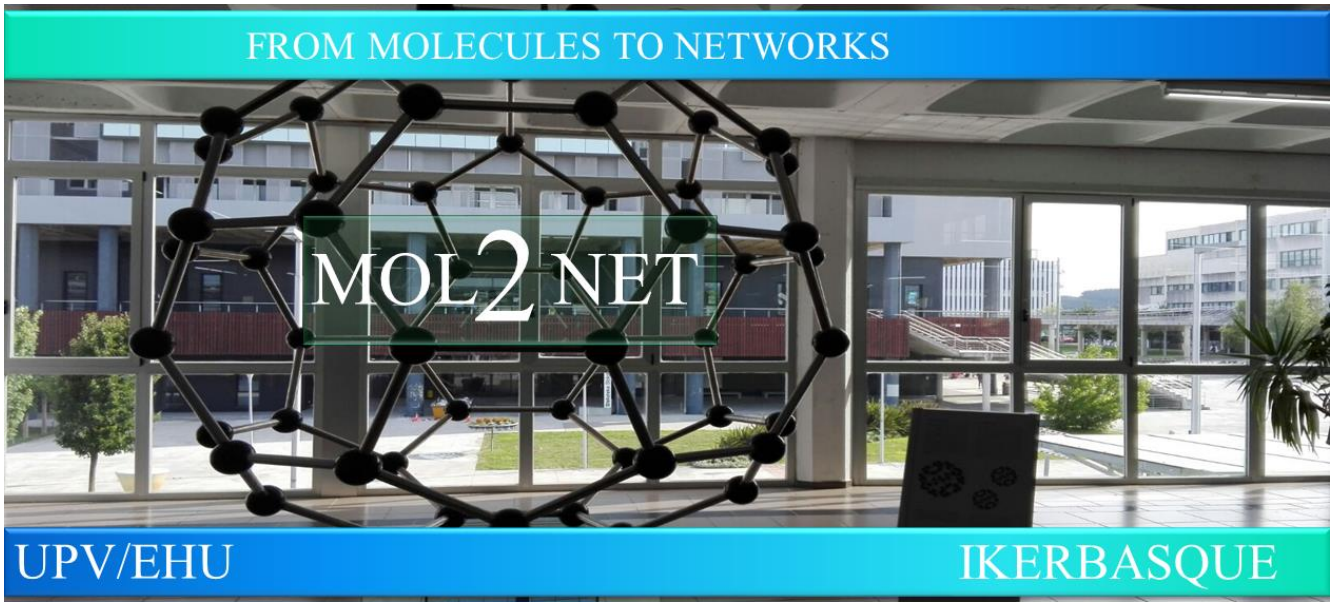

Molecular Topology Applied to Generate Pharmacokinetic Filters to Select Theoretical Antibacterial Compounds

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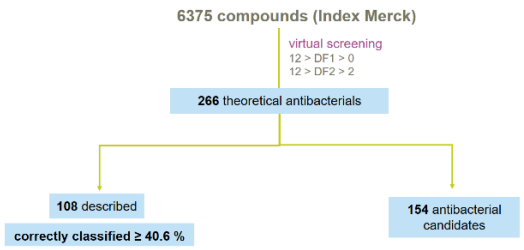
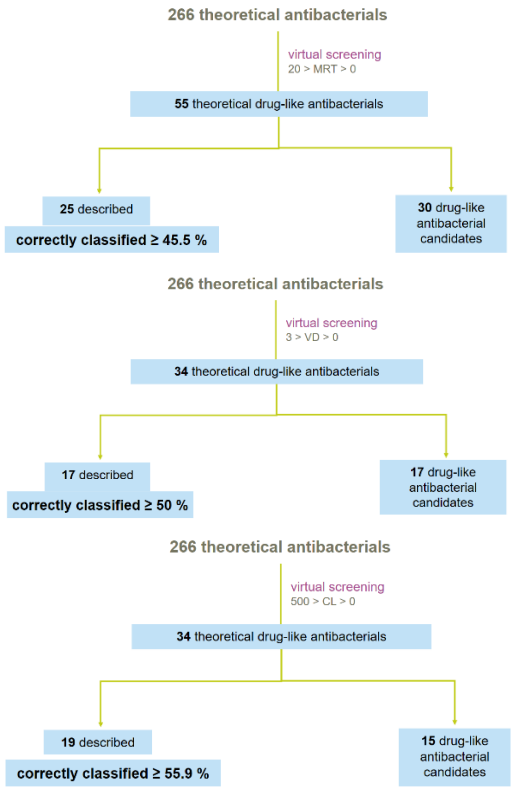
Graphical Abstract.



Abstract.

QSAR (Quantitative Structure-Activity Relationship) methods have been the basis for the design of new molecules with a certain activity. The great advantage of QSAR methods is that they are able to predict the pharmacological activity of compounds without the need to obtain or synthesize them previously.

Initially, drug design was a long and expensive process in which a vast number of compounds were synthesized and tested with a very low success rate. Virtual screening appears as a low cost solution to this problem by allowing researchers to identify molecules that are likely to be



active from a virtual library of thousands of compounds, allowing also the application of drug-like filters.

Currently, the development of antibiotic resistance by microorganisms is one of the most important problems that have appeared in recent years in the treatment of infectious diseases. This increased resistance is associated with increased morbidity and mortality from infections, as well as an increase in healthcare costs. The development of new molecules with antibacterial activity is therefore urgently needed.

By means of molecular topology, we developed discriminant functions capable of predicting antibacterial activity (DF1 and DF2). When applied to a database with 6375 commercial compounds, they selected 266 compounds as candidates from which 40.6 % have this activity according to bibliography. Regression equations determining pharmacokinetic properties such as mean residence time (MRT), volume of distribution (VD) and Clearance (CL) were applied as filters to the selected molecules, reaching a bibliographic success rate of 45.5, 50.0 and 55.9 %, respectively, which proves the usefulness of these mathematical-topological filters.

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