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TITLE

IS NATURAL PRODUCT DOMAIN A GOOD HUNTING HUB IN THE NAVIGATION OF DRUG LIKE AND DRUG MOLECULES?

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Natural products have been the source of inspiration in drug discovery for they have proven to be the richest source of novel compounds and new efficient drugs. Natural products display unique diversity in architecture and biological properties and are considered to have astonishingly smart pharmacokinetic profiles. These features make them highly privileged and interesting to explore them for drug design in the identification and development of new leads. To provide a guide for the identification of drug like natural products, a novel method to calculate quantitative score of drug likeness is required. A measure that characterizes similarity of natural product molecules to the structural space covered by bioactive molecules. The parameters considered for this computational score are the structural novelty, biodiversity, scaffold technologies and pharmaceutical relevance. The physicochemical descriptors of natural products and their typical structural features are compared to those of bioactive molecules to analyze the substructure of natural products with a particular focus on comparing the bioactive natural product scaffolds with those of new natural product entities for lead discovery, optimization and to derive consensus conclusions. A systematic structure oriented organizing principle of the known natural products combined with annotations of biological origin and pharmacological activity would chart the regions of chemical space explored by natural products provide a structural rationalization and categorization of natural product diversity, also provide guidance for the development of natural product like compound libraries. Drug like combinatorial libraries can be generated from combination of natural product like scaffolds and drug like functional groups. The current challenge is to design small molecule natural product libraries and methods to synchronize rational approaches especially those based on molecular modeling and chemo informatics for identification of natural product leads. The method of feature extraction to get constitutional finger prints of natural products along with other calculated descriptor values can be a good starting point for similarity based property calculations. Using several molecular properties and diversity indices the diversity of a library is estimated. Drug likeness can be quantitatively estimated by simple interpolation rather than recomputing the principal properties of new natural product chemical entities. Bioactive compounds share common pharmacophoric features and natural products provide a rich source of potentially attractive scaffolds and molecular building blocks for synthesis. A critical question to be answered in the near future is how to translate natural product complexity into plausible applications in pharmaceutical industry. One possibility is to focus on areas in chemical space that are populated by both synthetic drugs and bioactive natural products. It is more likely that the chemical space populated by bioactive natural products is greater than the areas covered by today's synthetic drugs. Certainly we have just begun to explore natural product diversity by computational means and there is lot of scope for stretching further. Our approach strives to identify new lead compounds by effectively employing computational tools on natural product libraries.