[P25] Natural product compound databases Diversity and applicability analysis for Virtual Screening

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In medicinal chemistry natural products (NPs) refer to molecules that are produced by a living organism but that do not directly contribute to its growth, development or reproduction [1]. The ability to synthesize a given NP is confined to different degrees in nature and the study thereof is the basis of chemotaxonomy [2]. Synthesis of such molecules is always tied to a cost, in respect to different resources, so that a physiological role must be fulfilled to comply with evolution [3]. For example, NPs participate in ecological interactions such as defense and intra- and interspecies communication. Therefore, they fall into the biologically relevant chemical space and are also considered privileged structures for drug discovery [4]. As compared to synthetic compounds NPs have been shown to possess a wider structural diversity that is also reflected in their molecular properties. It has been shown for instance that the steric complexity and the number rings per structure are higher in NPs [5-8]. Nevertheless, they lost attraction with the onset of high throughput screening (HTS) methods as they were deemed incompatible [9]. In light of their benefits and as certain disadvantages associated with NPs have become of lesser concern the use of this traditional drug resource has become more frequent in the search for innovative leads. One of the reasons is the routinely use of Virtual Screening (VS) which allows for a drastic reduction in candidate ligands by focusing on a few individual compounds for testing [10]. The compound libraries that can be used in VS have scarcely been studied themselves and their contents rarely compared [11,12,13,14]. In this study, an overview over 51 freely available NP and metabolite databases is provided. The data was downloaded, standardized, physicochemical descriptors and ADMET properties calculated and REOS and PAINS filters applied. The results were compared to approved FDA drugs, approved FDA NP drugs and drug-like datasets. Two independent VS were performed and the individual performances evaluated. The detailed description of these databases and the strategies chosen could assist in the design of NP VS by providing viable resources and strategies while deepening our understanding of NPs as such.

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