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Opinion Article

The Growth of Natural Medicines: Advancements and Chances

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DESCRIPTION

Pharmacotherapy has historically relied heavily on natural products and their structural analogues, particularly for the treatment of cancer and infectious diseases. However, the pharmaceutical industry has decreased its interest in natural products since the 1990s due to technical barriers to screening, isolation, characterization, and optimization. Natural products also present challenges for drug discovery. Improved analytical tools, strategies for genome mining and engineering, and advancements in microbial culturing are just a few of the technological and scientific advancements that have addressed these issues and created new opportunities in recent years. As a result, there is renewed interest in natural products as potential drug leads, particularly for combating antimicrobial resistance. In this paper, we present a synopsis of the most recent technological advancements that are making it possible to discover drugs based on natural products, highlight a few examples, and talk about important opportunities.

Natural products (NPs) have historically been an important part of drug discovery, particularly for cancer and infectious diseases, but also for cardiovascular diseases (such as statins) and multiple sclerosis (such as fingolimod). When compared to conventional synthetic molecules, NPs have unique characteristics that present both advantages and challenges for the drug discovery process. The enormous variety of scaffolds and structural complexity of NPs distinguish them. When compared to synthetic compound libraries, they typically have a higher molecular rigidity, a higher number of H-bond acceptors and donors, lower calculated octanol–water partition coefficients (cLogP values, indicating higher hydrophilicity), and a larger number of sp3 carbon, oxygen, and nitrogen atoms. Differences like these can be beneficial; For instance, the higher rigidity of NPs may be helpful in the process of developing drugs that target protein–protein interactions. Indeed, "beyond Lipinski's rule of five," NPs are a significant supplier of oral medications. The rise in molecular mass of approved oral drugs over the past two decades demonstrates the growing significance of drugs that do not adhere to this rule. Evolution has structurally "optimized" NPs to serve particular biological functions, such as controlling endogenous defense mechanisms and interacting (often competing) with other organisms, which is why they are so important for cancer and infectious diseases. Additionally, their application in traditional medicine may offer insight into their safety and efficacy. In general, the NP pool contains more "bioactive" compounds that span a wider chemical space than typical synthetic small-molecule libraries do.

Despite these benefits and numerous examples of successful drug discovery, pharmaceutical companies have reduced NP-based drug discovery programs due to a number of disadvantages. A library of extracts from natural sources is typically used in NP screening, which may not be compatible with conventional target-based assays. Dereplication tools must be used to avoid rediscovering previously known compounds in order to successfully identify the bioactive compounds of interest. It may also be difficult to obtain sufficient biological material to isolate and characterize a bioactive NP. In addition, obtaining IP rights for (unmodified) NPs with relevant bioactivities can be difficult due to the fact that naturally occurring compounds in their original form may not always be patented (legal frameworks vary from country to country and are changing), whereas simple derivatives can be protected by patents. The regulations defining the requirement for benefit sharing with countries of origin of the biological material, framed in the 1992 Convention on Biological Diversity of the United Nations and the Nagoya Protocol, which entered into force in 2014, as well as recent developments regarding benefit sharing linked to the use of marine genetic resources, add an additional layer of complexity.

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