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Natural product medicines: A literature update

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ABSTRACT

Natural products represent major approach for the discovery and development of new drugs. An updated review on the natural products is lacking in the literature. So, in the present review, an attempt has made to pool the source of current natural product information for health care professionals, to update the detailed information about natural products, to generate data bank on latest medical and scientific studies on natural products, including medically active foods (nutraceuticals).

Keywords: Natural Products, Natural Medicines, Literature Survey.

INTRODUCTION

Biodiversity is a valuable source of novelty in-terms of potentially appreciated molecules and also a revolution of thought, an expended view promising to transform glimpses of reductionist research of the past years into portraits of active world of systems biology, where organisms develop, differentiate and begin to deviate from the norm [1-3]. The biodiversity of nature has progressed from time to time to yield a baffling variety of secondary metabolites. The first and for a long-time extract of natural product were the only available medicines to mankind based on its empirical observations and folklore.

According to the WHO, 80% of the world's population mainly those of developing countries depend on plant derivative medicines for their healthcare, which are mostly supplanted by pharmaceutical constituents in the Western world. Natural products continued to play a major role, and endogenous chemicals, such as the prostaglandins, steroids and peptide hormones, provided the pharmaceutical industry with additional natural inspiration for drug discovery during the 20th century [4]. An aggregate of 1184 new chemical entities (NCEs) received consent as pharmaceutical drugs during the survey of molecules discovered post 1970 [5]. In past only few people tried to review and report the natural products for the source of drugs discovery [6, 7]. So, in the present review an attempt was made to enlist all the sources of the natural products with their potential to act as a source to discover drugs for treating diseases in multiple domains.

Natural Products: Historical Perspective

The natural product use exclusively plants for therapeutics is as earliest and widespread as medicine himself. From the Sumerian civilization the beneficial usage of plants was reported and approximately 400 diverse plant species were used for medicinal drives before the 400 years of Common Era Hippocrates. In ancient traditional medicine systems such as Ayurveda, Chinese and Egyptian natural products played a prominent role. According to the World Health Organization (WHO), 75% of people globally still rely on plant centred traditional medicines for prime health care. A brief summary of history of natural product medicine is presented in Table 1.

Current status of Natural Products

Natural products have been playing a vital role in health care for decades. Since ancient times, natural products represent the main source of compounds employed in drug discovery and development. From thousands of years nature has been a rich resource of beneficial biological agents and remarkable number of recent drugs has been resulting from natural sources grounded for their traditional medicine value. Natural products have played central part in treatment and prevention of human diseases during thousands of years. Remedies based on natural substances come from different sources, among them terrestrial plants and microorganisms, sea macro and microorganisms, as well as terrestrial invertebrates and vertebrates. Nature opened promising avenues for the treatment of great variety of diseases by

providing the mankind with a diversity of small bioactive compounds. The top most marketing drugs from the last century have been developed from natural products (Taxol from *T. brevifolia*, vincristine from *Vinca rosea* and morphine from *Papaver somniferum* etc.).

The prominent revival of interest has been witnessed among academic world as well as pharmaceutical companies in recent years for natural products as novel drugs sources. Around 40% of recent drugs in practice have been developed from natural products.

Table 1: History of natural product medicine

Type	Description	Period
Ayurveda (knowledge of life)	Chinese traditional medicine introduced medicinal properties of plants and other natural products	Before 3000
Ebers Papyrus	A huge number of crude drugs from natural sources presented (e.g., gum arabic and castor seeds)	1550 BC
The Father of Medicine "Hippocrates"	Different plants and animals described that could be sources of medicine	460–377 BC
Theophrastus	Different plants and animals described that could be sources of medicine	370–287 BC
Pliny the Elder	Different plants and animals described that could be sources of medicine	23–79 AD
Dioscorides	Wrote De Materia Medica, which described more than 600 medicinal plants	60–80 AD
Galen	The botanical medicines practiced (Galenicals) made popular in the West	131–200 AD
Krauterbuch (herbals)	Presented information and pictures of medicinal Plants	15th century

Natural products can be defined as the products of natural backgrounds. Natural products include: (1) an complete organism (e.g., a microorganism, a plant or an animal) that has not been exposed to any type of treatment other than a simple course of preservation (e.g., drying), (2) part of an organism (e.g., an isolated animal organ, flowers or leaves of a plant), (3) part of an organism, exudates and an organism extract and (4) pure compounds (e.g., terpenoids, coumarins, alkaloids, glycosides, flavonoids, steroids, sugars, lignans, etc.) isolated from microorganisms, animals or plants [8]. However, in maximum cases the term natural products denotes to secondary metabolites, minor molecules (mol. wt <200 amu) made by organisms that are not firmly needed for the existence of an organism. Concepts of secondary metabolism consist of products of overflow metabolism as a result of nutrient limitation, shunt metabolism produced during idiophase, defense mechanism regulator molecules, etc. [9]. Natural products can be from any terrestrial or marine source: plants (e.g., paclitaxel (Taxol) from *Taxus brevifolia*), animals (e.g., vitamins A and D from cod liver oil), or microorganisms (e.g., doxorubicin from *Streptomyces peucetius*).

According to Cragg *et al.* 39% of the 520 novel accepted medicines during 1983 and 1994 were from natural products or their offshoots and 60–80% of anticancer and antibacterial medicines have natural product origins. According to Cragg *et al.* [10] around 60% drugs of natural origins was in experimental trials for the propagation of cancers. In 2001 of the 30 top selling medicines eight (paclitaxel, azithromycin, pravastatin, ceftriaxone, cyclosporin, clavulanic acid, cvamoxycillin, and simvastatin) were of natural products or their offshoots and these eight medicines collected a total of US \$16 billion in sale. In the "natural" pharmaceutical industry the natural products have a direct use, which is increasing rapidly in North America and Europe apart from natural product-derived modern medicine. The use of natural products in traditional medicine is being incorporated into the primary health care systems of Mexico, the People's Republic of China, Nigeria, and other developing countries. The usage of herbal drugs is once-more fetching more popular in the form of complementary and alternative medicine, food supplements and nutraceuticals.

Interest in herbal drugs and natural medicine is undergoing a renaissance in the present age. Higher plant derived products represent around 25% of the total number of clinically used drugs [11]. The plants and other natural products are excellent sources of novel molecular chemotypes and molecular diversity mainly in the zones where worthy synthetic molecules do not exist [12]. The natural products are still providing their reasonable portion of novel clinical candidates and drugs despite competition from other drug discovery methods. Between 1981 and 2002, 5% of the 1,031 new chemical entities accepted as drugs by the US Food and Drug Administration (FDA) were natural products and another 23% were natural-product-derived compounds [13] Fig. 1.

About 250000 living plant species cover a much greater variety of bioactive compounds than any chemical library made by humans.

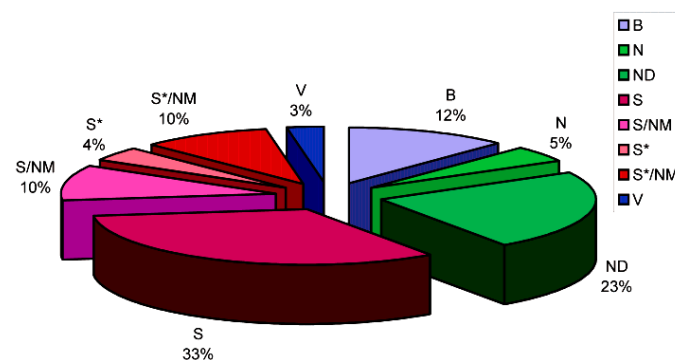


Figure 1: All new chemical entities by source between 1981-2002, (Total =1031)

"B": Biological; usually a large (>45 residues) peptide or protein either isolated from an organism/cell line or produced by biotechnological means in a surrogate host. "S": Totally synthetic drug, often found by random screening/modification of an existing agent. "N": Natural product. "S*": Made by total synthesis, but the pharmacophore is/was from a natural product. "ND": Derived from a natural product and is usually a semisynthetic modification. "V": Vaccine. "NM": Natural product mimic.

NATURAL PRODUCTS- FUTURE PROSPECTS

About one-half of all drugs in current use comprise of naturally occurring compounds and their derivatives. They have also provided the molecular template or intellectual stimulus for the synthesis of about half of all synthetically produced medicinal compounds. A statistical analysis of compounds isolated from natural products and those derived by total synthesis employed in drug development has shown that a mere 90,000 known naturally occurring compounds contribute about 40% of total possible new drug molecules, whereas the several millions of synthetic molecules account for the remaining 60%. This remarkable difference in productivity can be attributed to the fact that only a limited number of different molecules are involved in, or have a beneficial effect upon life processes, and that nature has performed a pre-selection of molecules that influence specific metabolic role in all living things. It is noteworthy that despite the large investment by the pharmaceutical industry in modern-drug-discovery technology, such as combinatorial chemistry and robotic-based High-Throughput Screening, natural products continue as one of the major sources of new structural entities for drug development. During the investigation of the isolated compounds from natural sources, new insights into the mechanism of drug action have been developed. In this connection, the annals of modern pharmacology have recorded impressive gains from natural products such as heroin, nicotine, acetylcholine, penicillin etc.

Since molecular structure is intricately linked to biological activity, for the medicinal chemist, the natural products represent a treasure trove of possibilities. When the mechanism of action of a compound is unknown, the synthesis and study of carefully designed analogs of the lead compound can be used to fine-tune the drug-molecular target interaction so as to produce the desired biological response. Lastly, lead modification is also employed simply to alter the physico-chemical characteristics of a given molecule so that the latter can be amenable to formulation (e.g., as an oral dosage form).

CONCLUSION

Based on the above review, it could be concluded that plants are a good source of natural product drugs. The natural products will enable the discovery of drugs to treat the deadly human diseases. Further work is needed to discover new natural products to replace the allopathic drugs.

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