Review Article

Medicinal Plants As A Potential Source For Drug Discovery

Subhash C Mandal[1*], S.A. Nirmal[2], S.C. Pal[3]

[1]Pharmacognosy and Phytotherapy Research Laboratory, Division of Pharmacognosy, Department of Pharmaceutical Technology, Jadavpur University, Kolkata-700 032.

[2]Department of Pharmacognosy, Pravara Rural College of Pharmacy, Loni, Maharashtra, India.

[3]Department of Pharmacognosy, NDMVP's College of Pharmacy, Nasik, Maharashtra, India.

*Corresponding author: subhashmandal@yahoo.com

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Abstract: Current report the drug discovery from medicinal plants involves a multifaceted approach combining botanical, phytochemical, biological, and molecular techniques. This search continues to provide with new and important leads against various pharmacological targets including cancer, HIV/AIDS, Alzheimer's, malaria, and pain. However, new drug discovery is facing serious challenges due to reduction in number of new drug approvals coupled with exorbitant rising cost. This scenario has prompted us to come out with a novel approach of integrated drug discovery, where Ayurvedic wisdom can synergize with drug discovery from plant sources. The starting point for plant-based new drug discovery should be identification of the right candidate plants by applying Ayurvedic wisdom, traditional documented use, tribal non-documented use and exhaustive literature search. Bioassay-guided fractionation of the extracts of identified plant may lead to isolated bioactive compound as the new drug. This integrated approach would lead to saving of cost and time, coupled with enhanced success rate in drug discovery.

Key words: Medicinal plants, Natural resources, Drug discovery, Pharmacognosy

Introduction

Plants have been utilized as medicines for thousands of years. Initially these medicines were taken in the form of crude drugs such as tinctures, teas, poultices, powders and other herbal formulations (Samuelsson, 2004). Information about the medicinal plants was recorded in books based on the oral knowledge passed down. Later on, phytochemistry, a branch of pharmacognosy was developed which suggested use of isolated active compounds from medicinal plants for the treatment of diseases and morphine was the first isolated compound from opium in the early 19th century (Kinghorn, 2001). Later on, other active compounds like cocaine, codeine, digitoxin, and quinine were also isolated (Newman *et al.,* 2000). Isolation and characterization of pharmacologically active compounds from medicinal plants continue even today.

Drug discovery from medicinal plants involves many people such as botanists, ethnobotanists, ethnopharmacologists and plant ecologists who collect and identify the plant(s) of interest. Collection may involve species with known biological activity for which active compound(s) have not been isolated (e.g. traditionally used herbal remedies). Phytochemists prepare extracts from the plant materials, subject these extracts to biological screening in pharmacologically relevant assays and commence the process of isolation and characterization of the active compound(s) through bioassay-guided fractionation. In this context, molecular biology has also become essential to medicinal plant drug discovery through the determination and implementation of appropriate screening assays directed

towards physiologically relevant molecular targets. Pharmacognosy encapsulates all of these fields involved in the process of drug discovery from medicinal plants.

The definition and practice of pharmacognosy have been evolving since the term was first introduced about 200 years ago (Kinghorn, 2001). The American Society of Pharmacognosy refers to pharmacognosy as "the study of the physical, chemical, biochemical and biological properties of drugs, drug substances or potential drugs or drug substances of natural origin as well as the search for new drugs from natural sources". As practiced today, pharmacognosy involves the broad study of natural products from various sources including plants, bacteria, fungi and marine organisms. It includes the search for single compound drug leads that may proceed through further development into Food and Drug Administration (FDA)-approved medicines.

Challenges in drug discovery from medicinal plants

Despite the evident successes of drug discovery from medicinal plants, future endeavors face many challenges. Pharmacognosists, phytochemists and other natural product scientists will need to continuously improve the quality and quantity of compounds that enter the drug development phase to keep pace with other drug discovery efforts (Butler, 2004). The process of drug discovery has been estimated to take an average of 10 years upwards (Reichert, 2003) and cost more than 800 million dollars (Dickson and Gagnon, 2004). Much of this time and money is spent on the numerous leads that are discarded during the drug discovery process. In fact, it has been estimated that only one in 5000 lead compounds will successfully advance through clinical trials and get approved for use; lead identification is the first step in a lengthy drug development process. Lead optimization (involving medicinal and combinatorial chemistry), lead development (including pharmacology, toxicology, pharmacokinetics, ADME [absorption, distribution, metabolism and excretion] and drug delivery) and clinical trials, all take a considerable length of time (Fig. 1).

Drug discovery from medicinal plants has traditionally been lengthier and more complicated than other drug discovery methods. As such, many pharmaceutical companies have eliminated or scaled down their natural product research (Koehn and Carter, 2005). In addition, research and development related to medicinal plant and natural product drug discovery in academic pharmacy departments is declining. On the other side, many research organizations have come forward for natural products search. As drug discovery from medicinal plants is time-consuming, as explained above, faster and better methodologies for plant collection, bioassay screening, compound isolation and compound development must be applied (Do and Bernard, 2004).

The design, determination and implementation of appropriate, clinically relevant, high-throughput bioassays is a difficult process for all the drug discovery programs (Knowles and Gromo, 2003). Still, with a proper design of high-throughput screening assays, one can screen compounds and extract libraries for biological activities (Walters and Namchuk, 2003). New techniques including pre-fractionation of extracts can solve many problems. Challenges in bioassay screening still remain as an important issue in the future of drug discovery from medicinal plants. Improving the speed of active compound isolation will necessitate the incorporation of new technologies. Although Nuclear Magnetic Resonance (NMR) and Mass Spectrometry (MS) are currently in wide use for compound identification, new methods of using NMR and MS could be applied to medicinal plant drug discovery to facilitate compound isolation (Eldridge *et al.*, 2002; Pellecchia *et al.*, 2002; Glish and Vachet, 2003). Also, high-throughput X-ray crystallography could be applied to medicinal plant lead discovery (Blundell *et al.,* 2002).

Compound development of drugs discovered from medicinal plants also faces unique challenges. Natural products are present only in small quantities in to the plants and hence, after their isolation, the quantity derived is insufficient for lead optimization, lead development and clinical trials. So, collaboration with synthetic and medicinal chemists is necessary to determine whether synthesis or semi-synthesis is required

(Lombardino and Lowe, III, 2004). Natural product and natural-product-like libraries can be developed that combine the features of natural products with combinatorial chemistry to improve the natural product compound development (Ganesan, 2004).

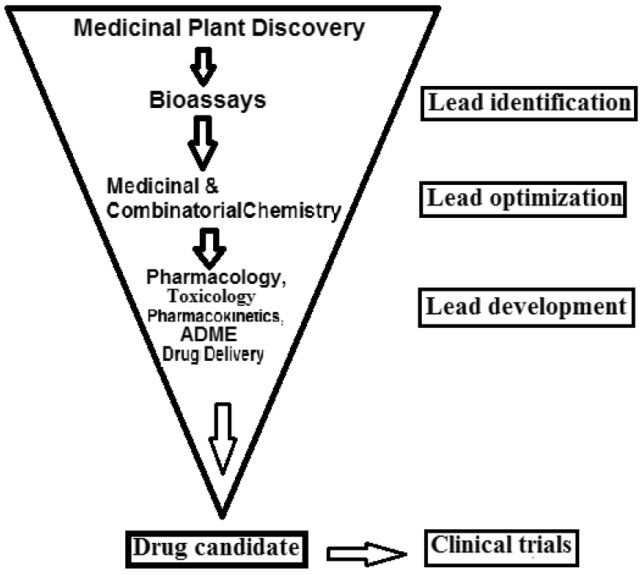

Fig. 1. Typical medicinal plant drug discovery and development process. (Figure courtesy of Dr. Robert W. Brueggemeier, College of Pharmacy, The Ohio State University)

Drug discovery through ethnobotanical approach is one of the better routes for finding out new lead molecules (Mandal *et al.,* 2002) and many medicinal plants occurring in Arunachal Pradesh, India have promising traditional uses and could serve as potential sources for lead molecules (Namsa *et al.,* 2011). Ayurveda is the most ancient alternative medicine system developed in India that has unearthed many potential drugs for the treatment of diseases and there is tremendous scope for drug discovery using the Indian traditional system (Nirmal *et al.,* 2011). Herbal formulations are very effective in the treatment of diseases and their efficacy can be improved by various methods for better treatment (Bhattacharyya *et al.,* 2011).

Advantages of drug discovery from natural resources

1. The drugs are obtained from the medicinal plants have long term use in humans. It mean that such drugs are safe for human use. Once proved, synthesis of such drugs can be done to reduce the pressure on the natural resources.
2. Such approaches sometimes lead to the isolation of novel molecules from the sources due to the limitations of the original molecules e.g. podophyllin derived from *Podophyllum hexandrum* had dose-limiting toxicities. Such limitations could be overcome to a great extent by the semi-synthesis of etoposide, which continues to be used in cancer therapy today. Similar was the case with camptothecin which led to the development of novel anticancer molecules like topotecan and irinotecan.
3. Natural resources can give original molecules or semi synthetic molecules to overcome the inherent limitations of the existing drugs.

Disadvantages of drug discovery from natural resources

1. Commercialization of drug discovery from plants pressurizes the resource substantially and might lead to undesirable environmental concerns. it is expected that some 25,000 plant species would cease to exist by the end of this century.
2. Over a period of time, the Intellectual Property Rights (IPR) protection related to the natural products is going haywire and this process of accessing the basic lead resources have become highly complex in many countries. These processes tend to impede the pace of discovery process at various phases, irrespective of the concerns, leading to such processes (Mahidol *et al.,* 1998).

Conclusion

There is a pertinent need to renew scientific enthusiasm towards natural products for inclusion in the drug discovery program. Documented clinical experience with botanical medicines as codified in traditional systems of medicine might simplify the issues associated with poor predictability. It is time for large-scale pharmaceutical organizations to open up the developmental strategies. In view of the increasing cost of development of new drugs, alternative approaches like development of herbal extracts hitting multiple targets as new drugs need to be immediately considered. Obviously, the cost

of development shall be substantially lower in case of herbal extracts. Such strategy would not only enhance the chances of success in terms of providing effective and safe drugs but also it will minimize the risk of post-marketing withdrawals. Such a complementary scenario shall go a long way in safeguarding the interests of both pharmaceutical industry and common man. In conclusion, natural products discovered from medicinal plants and their derivatives have provided with numerous clinically used medicines. Even with all the challenges posed to the drug discovery from medicinal plants, natural products isolated from these plants can be predicted to remain as an essential component in the search for new medicines.

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