INTRODUCTION

Plant has been utilized as medicine for 1000's of year. These medicines initially took the form of crude drugs such as tinctures, teas, poultices, powders, and other herbal formulations. The specific plant to be used as and the method of application for particular ailments were passed down through oral tradition. Eventually information regarding medicinal plant was recorded in herbal pharmacopoeia.

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The World Health Organization (WHO) estimated that 80% of the population of developing countries relies on traditional medicines, mostly plant drugs, for their primary health care needs. Also, modern pharmacopoeia still contains at least 25% drugs derived from plants and many others which are synthetic analogues built on prototype compounds isolated from plants. Demand for medicinal plant is increasing in both developing and developed countries due to growing recognition of natural products, being non-narcotic, having no side-effects, easily available at affordable prices and sometime the only source of health care available to the poor. Medicinal plant sector has traditionally occupied an important position in the socio cultural, spiritual and medicinal area of rural and tribal lives of India.

Medicinal plants as a group comprise approximately 8000 species and account for around 50% of all the higher flowering plant species of India. There are estimated to be over 7800 manufacturing units in India. In recent years, the growing demand for herbal product has led to a quantum jump in
volume of plant materials traded within and across the countries. According to an all India ethnobiological survey carried out by the Ministry of Environment & Forests, Government of India, there are over 8000 species of plants being used by the people of India.

Indian Vedas describe the widespread use of herbal products and aqueous extract of different plant parts for curing different disease. Maximum 30% of root part of medicinal plant is used in different practices in compression to other plant parts\(^1\).\(^3\).

Historically, the majority of new drugs have been generated from natural products (secondary metabolites) and from compounds derived from natural products. During the past 15 years, Pharmaceutical industry research into natural products has declined, in part because of an emphasis on high-throughput screening of synthetic libraries. Currently there is substantial decline in new drug approvals and impending loss of patent protection for important medicines. However, untapped biological resources, “smart screening” methods, robotic separation with structural analysis, metabolic engineering, and synthetic biology offer exciting technologies for new natural product drug discovery. Advances in rapid genetic sequencing, coupled with manipulation of biosynthetic pathways, may provide a vast resource for the future discovery of pharmaceutical agents\(^4\).

**Importance and scope of medicinal plants**

Not only in India, but in many other countries plants have played significant and prominent role as medicine. In the third world countries, even today, medicinal needs of about 80 per cent people are met by crude-herbal preparations. At one time, it was felt that the chemical synthesis would completely replace the drugs of natural origin. Notwithstanding the great discoveries in the field of synthetic drugs, the use of plant drugs (e.g. quinine, morphine, vinblastine, and vincristine) remained unabated. Furthermore, inspite of the emergence of many wonder drugs from the synthetic field, the problems of senescence and so called ‘civilization’ diseases, e.g. immunodeficiency syndromes, arthritis, mental disorders and cancer, cannot be tackled and therefore, there is a greater demand for natural medicines and ‘health-foods’ today than ever before in the world.

The essential oils are used in every-day human-life in various ways and their consumption is rapidly increasing. A few of the common uses to which essential oils and their derivatives are put to, are in the manufacture of soaps, cosmetics, pharmaceutical preparation, confectionery, aerated waters, disinfectants, detergents, incenses, etc. India was at one time famous for the manufacture and distillation of high quality perfumes and scents. According to an estimate, 1000 different aromatic plants out of a total of 1500 varieties used in perfumery throughout the world are found in India.

The economic importance of both these groups of medicinal and aromatic plant can be gauged from the fact that 25 years ago vegetable drugs worth million of rupees were used to be exported from India. This trade dwindled later because of exporting unstandardized and adulterated material. The trade can be revived if steps are taken to produce and export material of standard quality. On the other hand, a considerable quantity of crude drugs is imported from foreign countries for the use of pharmaceutical industry in India. Systematic exploitation of these two groups of plants by the Indian Pharmaceuticals Industry, therefore, will bring great economic advantage to the country. These plants are now being utilized in the practice of medicine in this country and are also exported to foreign countries.

In the medicinal plants sector, the World Health Organization (WHO) has estimated that about 80 per cent of the population of developing countries rely on the modern medicines that also contain about 25 per cent drugs derived from plants. On account of the fact that derivatives of medicinal and aromatic plants are non-narcotic having no side effects, even if used for a prolonged time in permissible doses, the demand for these plants is on the increase in both developing and developed countries. There are, estimated to be around 25000 effective plant based formulations available under the indigenous medicine. Over one and a half million practitioners of the Indian System of Medicine in the oral and codified streams are medicinal plants
in preventive, promotive and curative applications. There are, estimated to be over 8000 manufacturing units, which use plants as raw material for preparing medicines. As estimated by the Exim Bank (1998), the international market of medicinal plants related trade is to the tune of US $60 billion per year having a growth rate of 7 per cent per annum. The annual exports of these plants are valued at Rs. 1000 crores. As per estimates by National Medicinal Plant Board the annual growth in several herbs is between 15-30 per cent.

The aromatic plants provide the raw material for the production of flavours, condiments, herbal cosmetics, perfumery, scented soaps, hair oils, aerated water, etc. Demand for these herbs is increasing progressively with increase in number of star hotels and multinationals establishing consumer oriented cosmetics, biscuits and pharmaceutical units. Currently, most of these herbs are grown in large quantities and marketed by France, U.K., Canada, Turkey and U.S.A. It is estimated that Indian consumption alone of these herbs is approximately 200 tones per annum, and only about 60 tonnes are produced indigenously. Bulk of these herbs (188 tonnes) is used for culinary purposes and about 12 tonnes are consumed for medicinal and cosmetic preparations. The annual exports of the derivatives from these plants are to the tune of Rs. 600-700 million.

 Drugs from nature-past achievements, future prospects

Most drugs have been derived from natural products, but there has been a shift away from their use with the increasing predominance of molecular approaches to drug discovery. Nevertheless, their structural diversity makes them a valuable source of novel lead compounds against newly discovered therapeutic targets. Technical advances in analytical techniques mean that the use of natural products is easier than before. The drug discovery from natural source makes use of material that has been found by trial and error over many years in different cultures and systems of medicine. Examples include drugs such as morphine, quinine and ephedrine that have been in widespread use for a long time, and more recently adopted compounds such as the antimalarial artemisinin.

Some of the prominent commercial plant-derived medicinal compounds include: colchicum, colchicine, betulinic acid, camptothecin, topotecan (Hycamtin®), CPT-11 (irinotecan, Camptosar®), 9-aminocamptothecin, delta-9- tetrahydrocannabinol (dronabinol, Marinol®), beta lapachone, lapachol, podophyllotoxin, etoposide, podophyllinic acid, vinblastine (Velban®), vincristine (leurocristine, Oncovin®), indesine (Eldisine®, Fildesin®), vinorelbine (Navelbine®), docetaxel (Taxotere®), pacilitaxel (Taxol®), tubocurarine, pilocarpine, scopoline. The Natural products research continues to explore a variety of lead structures, which may be used as templates for the development of new drugs by the pharmaceutical industry.

Natural products have been optimized over long time periods against their gene product. Therefore, therapeutic effects of natural product-derived drugs are predominantly achieved in antibiotic therapies; oncology and immunoregulation higher hit rates are generally obtained for natural product libraries in HTS campaigns compared to medicem or combichem libraries. Natural products are a valuable source of unsurpassed structural diversity and functional density to identify screening hits.

The recent adoption of biochemical assays and high-throughput screening has created the illusion that natural extract screening is somehow less effective or less practical than the high-throughput screening of large corporate compound collections. In fact, it is the high-throughput biochemical screening paradigm that has exceeded its own practicality. Laboratory investigations and clinical studies around the world are performed to confirm the efficacy of many plant extracts and micronutrients. It is the rare case indeed that rigorous data demonstrate bioavailability, exposure, delivery, and dose-dependent efficacy. However, it is likely that in the near future, these hopeful studies will begin to bear fruit in the clinic.

Even with lack of support from the major pharmaceutical companies, natural products still show a substantial impact on the drug discovery process. At least 23 natural product and natural-
product-derived drugs have been launched onto the
market in Europe, Japan or the United States
from 2001 to 2005. Furthermore, a total of 136
natural product and natural-product-derived drugs
have undergone various stages of clinical
development in all major therapeutic areas. Some
of these clinical candidates will be launched onto
the market to treat human diseases. It is interesting
to note that all antibacterial and antifungal clinical
candidates of natural product origin were derived
from microbial sources.10

Different approaches with natural product
Mainly there are three different approaches as
1. Traditional
2. Empirical
3. Molecular

Traditional
THE R&D thrust in the pharmaceutical
sector is focused on development of new drugs,
innovative/indigenous processes for known drugs
and development of plant-based drugs through
investigation of leads from the traditional systems
of medicine. Ayurveda is a traditional Indian
medicinal system being practiced for thousands of
years. Considerable research on pharmacognosy,
chemistry, pharmacology and clinical therapeutics
has been carried out on ayurvedic medicinal plants.
For ayurveda and other traditional medicines newer
guidelines of standardization, manufacture and
quality control are required. Employing a unique
holistic approach, ayurvedic medicines are usually
customized to an individual constitution. Traditional
knowledge-driven drug development can follow a
reverse pharmacology path and reduce time and
cost of development.11

Molecular
The molecular approach to drug discovery
can be further subdivided into three general
categories. The first is rational drug design using
computer-aided techniques. A second area is the
antisense approach, which is based on manipulation
of genetic targets. The third technique, which
currently dominates drug discovery activity, is the
HTS. Over the past ten years, many biochemical
assays have been adapted for use on 96-well
microplates, and more dense formats are becoming
common. This has enabled enormous increases in
throughput to be achieved, but this in itself creates
new problems.12

Need of natural product research
Throughout the world in current research
scenario, the development of a new drug entity with
promising efficacy and less toxicity for treatment of
various incurable ailments requires huge
investment and longer period for clinical trials. Drugs
from natural sources are considered to be a
promising solution to serve the purpose. Among the
diversity of most natural products, medicinal plants
are still the most favorable for the scientist to explore
a new drug.13

Difficulties of natural product (NP) versus
synthetic chemicals
Four converging factors have brought
pressure to bear on natural product programs over
the past decade:
- Most ‘easy-to-find’ antibacterial, antifungal
  and antitumor NPs had been found, and so
  many programs have relied heavily on
dereplication programs to find new NP
chemical entities for old ‘cytocidal’ targets.
- As the pharmaceutical industry has become
  more sophisticated, progressing from cell-
based killing assays to more
pharmacologically relevant enzyme
inhibition, receptor-based assays, protein–
protein interactions and other biochemically
oriented assay systems, NP extracts have
been broadly deemed as too ‘dirty’, too
difficult to assay or too time-consuming to
be competitive with companies’ chemical
collections.
- In an increasingly fast-paced drug discovery
  process led by the development of
roboticized HTS, the time taken to progress
from an NP assay hit to knowing its chemical
structure (in the past, this was often
measured in months) has put NPs at a
significant disadvantage compared with
synthetic chemicals for which the structures
are already known.
- Medicinal chemists requested to derive
  optimized drugs from such leads often view
  NPs as ‘ugly ducklings’, possessing
undesirable features such as structural
complexity, multiple hydroxyl moieties,
ketones and chiral centers. Many NP programs have only successfully competed in pharmacological and biochemical assays when used as a last resort after failure of synthetic chemical collections to produce chemical entities possessing a high enough potency. As a result, in some cases, NP programs have remained strongly aligned with dwindling anti-infective, anticancer or agricultural programs, possibly to the detriment of both sides.\textsuperscript{14}

Seven routes to success with natural products

Natural product screening

In response to the competition from synthetic libraries, the process of natural product screening has certainly been streamlined.

Unnatural' natural products

While the traditional screening of natural product extracts will continue to reveal exciting leads, another avenue is the manipulation of biosynthetic pathways to produce novel natural products.

Natural products as a source of building blocks

Some natural products are available cheaply and abundantly. These are degraded to provide a set of chiral building blocks that are then assembled into novel combinatorial scaffolds.

The derivatization of natural products

Besides degradation to fragments, readily available natural products can be exploited by combinatorial derivatization.

Natural-product analogues by total synthesis

Here, the primary objective is to increase our knowledge of the natural product's SAR to discover improved analogues with enhanced biological and/or pharmacokinetic properties.

Natural products as a source of scaffolds

In recent years, numerous academic groups have targeted the combinatorial investigation of natural product scaffolds as starting points for novel leads.

Natural-product-like libraries

The final approach is revolutionary, in that it aims to create truly synthetic molecules that resemble natural products. Such libraries are usually composed around a cyclic scaffold, and embrace a high degree of stereochemical content.\textsuperscript{15,16}

CONCLUSIONS

Despite a period in which pharmaceutical companies cut back on their use of natural products in drug discovery, there are many promising drug candidates in the current development pipeline that are of natural origin. Technical drawbacks associated with natural product research have been lessened, and there are better opportunities to explore the biological activity of previously inaccessible sources of natural products. With the increasing acceptance that the chemical diversity of natural products is well suited to provide the core scaffolds for future drugs, there will be further developments in the use of novel natural products and chemical libraries based on natural products in drug discovery campaigns.

ACKNOWLEDGEMENTS

The author is grateful to principal of A.B.C.P. Sangli, Maharashtra for providing necessary facilities and also deeply acknowledges Mrs. Nikewade N.S, Mrs. Tanvade S.S. & Mr. P.J. Shirote for the technical advices. I also thanks to all colleagues.

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